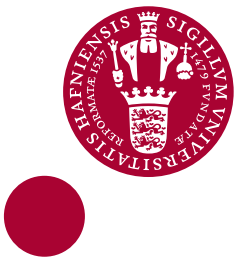

Beyond "Good Governance"

Trust, Consent, Exploitation and Vulnerability in Cross-Cultural Biobanking

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Academic advisor: Klemens Kappel

Submitted on: 21 April 2017

Beyond “Good Governance”:
Trust, Consent, Exploitation and Vulnerability in Cross-Cultural Biobanking

PhD Thesis
By Nana Cecilie Halmsted Kongsholm

University of Copenhagen
Department of Media, Cognition and Communication
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For my father,
Henning Kongsholm
(1946-2016)

Table of Contents

Co-authorship

Article 1 is co-authored by Jesper Lassen and Peter Sandøe.

I am responsible for the collection, transcription and analysis of interview data, and for developing and drafting the manuscript.

Jesper Lassen and Peter Sandøe have both contributed with supervision in qualitative methods (semi-structured interviews), in analysis and interpretation of data, and with substantial critical discussion and revision of the manuscript.

Article 2 is co-authored by Klemens Kappel.

I am responsible for the development and drafting of the manuscript.

Klemens Kappel has contributed with development of ideas and arguments, as well as substantial critical discussion and revision of the manuscript.

Introduction

This dissertation explores four concepts and their interrelation as they pertain to medical research; namely those of trust, consent, exploitation, and vulnerability. Based on an empirical study of motivations, expectations and strategies among biobank donors and researchers in rural Pakistan (Article 1), I defend the notion and practice of trust-based consent to participation in medical research (Article 2), and develop a novel conception of the relation between exploitation, vulnerability and consent in the context of medical research (Article 3).

My PhD project is part of the interdisciplinary research project *'Global Genes, Local Concerns'* (GGLC). Built around an existing collaboration between the University of Copenhagen (UCPH) and the National Institute for Biotechnology and Genetic Engineering (NIBGE) in Faisalabad, Pakistan, the overall aim of the GGLC project has been to explore and find solutions (ideally in the form of ethical guidelines) to the scientific, legal and ethical challenges met by cross-national biobanking.

The collaboration between NIBGE and UCPH is centered on the exchange of and research on blood samples from donors with otherwise rare genetic disorders, which, due to the local practice of consanguineous marriages, are nonetheless highly prevalent in the areas surrounding NIBGE. Through the collaboration the UCPH researchers gain unique access to research material of a nature and extent that would otherwise be difficult to procure; and the NIBGE researchers gain access to advanced technologies and research opportunities in Denmark, that are not present or accessible in Pakistan.

The original aim of my PhD project was to investigate the ethical challenges arising from biobanks operating across diverse ethical norms and values. Using the UCPH-NIBGE collaboration as a case study, the aim was to explore the ethical issues that arise in the collection and exchange of samples between Denmark and Pakistan – two countries that are vastly different with respect to legislation, medical infrastructure, and moral thinking. These ethical issues were expected to be related to the interpretation of the requirements for informed consent; norms regarding how potential benefits of biobanks should be used; stigmatization of vulnerable populations; and gender and group identities. However (and as is the case in many PhD projects), this focus was modified during the progression of the project, not least due to the empirical study that turned our attention to other issues. Nevertheless, in the following I will give an account of the theoretical starting point of the project, to make clear how and why this later modification took place, and what influenced it.

The initial theoretical trajectory of the project was guided by a number of issues and assumptions rooted in moral philosophy and bioethical debate. First, we had the assumption that the highly hierarchical structures generally prevalent in Pakistani society – manifested e.g. in that authority accorded with gender and age (Zaman 1992) – would have a negative impact on autonomy of the individual, an essential element in consent to participation in medical research (Beauchamp & Childress 2001). In this way, we expected decision-making of Pakistani women and young adults to be subsumed under the authority of their husbands and/or elders – a matter which would be ethically problematic from the point of view of accounts of the notion and value of autonomy in both medical ethics specifically (see e.g. World Medical Association 1964, Levine 1986) and moral philosophy generally (see e.g. Mill 1859; Berlin 1969). Furthermore, individuals' reliance on and deference to such authority holders in making decisions for them (evidenced also in the practice of collective consent, see e.g. Tindana et al. 2011, Ganguli-Mitra 2008a) were suspected to potentially result in paternalistic decision-making structures regarding health matters – something to be avoided, according to leading accounts in moral theory and medical ethics alike (Dworkin 1972, Eyal 2012b, Faden & Beauchamp 1986).

Second, we expected the prominent role of religion in the Pakistani society to be a source of potential conflict when juxtaposed with 'Western' and secular moral and scientific norms, and in turn in the development of legitimate policies. This was in particular in relation to two matters:

1) In Pakistan, scientific and medical questions regarding health, life and death is understood in religious terms (Moazam 2000). We expected this to complicate communication and discussion regarding sample collection (e.g. regarding storage of samples after the donor's death).
2) In contrast to secular societies, in Pakistan moral and ethical obligations are derived from Islam – very simply put, religion and ethics are assumed to be two sides of the same coin (this is evident e.g. in that bioethical dilemmas are settled through religiously informed *fatwas*; see below). Thus, appeal to moral norms (e.g. autonomy and justice), as isolated, abstract principles would seem alien in this context.

These two aspects of the intellectual landscape in Pakistan stand in contrast with a dominant secular framework for societal decision- and policy-making, exemplified by John Rawls' theory of political liberalism (1993). Here, Rawls draws a line between the *public sphere* and the *background culture*: whatever religious or moral doctrines citizens may adhere to, belong to the background culture of civil society and are not to be influent in political decision-making. In contrast, the proper site of political activity is the public sphere, *"guided by* […] *principles and values of which all citizens can endorse* […] *presented as freestanding and expounded apart from, or without reference to, any* […] *wider background"* (Rawls 1993, pp. 10-12).

Third, the two above issues point to an overarching challenge of what we may call ethical and cultural incommensurability; one that has spawned general criticism of the Rawlsian framework as accounted for above (see e.g. Kymlicka 1989, Benhabib 2002, Bohmann 1995). The claim is that the level of abstraction in reasoning about political matters that Rawls demands is unattainable: many cultures simply cannot separate public and background reasons, as their mode of reasoning is contingent on and informed by culture (and in many cases, religion). Thus, they may not be able to separate "public" and "background" reasons in policy-making, as these two are historically woven together.

Insisting on keeping 'public' and 'background' reasons separate may have ramifications for the ethical validity and quality of policies: the level of abstraction in reasoning about societal and political matters demanded by Rawls' political liberalism may ignore the highly historically and culturally contingent nature of both reasons and reasoning with some cultures. And in the context of decision-making, enforcing practices that would provide for ethically valid, i.e. autonomous, decisions on the account of dominant theories in medical ethics – such as insisting on obtaining consent from each individual – could likely violate established ethical norms and standards regarding elder authority in a Pakistani context.

On the other hand, this approach may be described as largely relativistic[1] and criticized on this account: uncritically according authority to procedures and practices with no other justification other than that they are an expression of a given culture's established reasons and beliefs may result in a too-inclusive permissiveness, approving practices and procedures that harm individuals (within the present context, this dilemma is exemplified by the debate on whether the cultural practices of elder or collective consent may in fact harm individuals' interests, see e.g. Kamuya et al. 2011, Gikonyo et al. 2008, Dawson & Kass 2005).

In this dissertation I take no stance on he matter of relativism as such. However, my investigation, particularly bolstered by the empirical study, leads me to the provisional stance that in concrete contexts

[1] Relativism refers to the view that truth and falsity, standards of reasoning and procedures of justification are products of differing conventions, and their authority is confined to the context giving rise to them.

there are both pragmatic and ethical reasons for paying close attention to the background culture. This is not least the case in international research relations and collaborations. I elaborate upon this issue in Article 3.

As a means to investigate these theoretical issues "on the ground", we traveled to NIBGE and conducted interviews with families from the villages surrounding the institute, who had all given samples to the institute, and with NIBGE researchers who had experience in collecting samples from families. This empirical study is detailed in Article 1. The interviews with donors and our interactions with the researchers turned our attention to ethical matters in the sample collection and exchange that we had not considered previously. Conversely, our empirical investigation made us realize that the questions and issues that initially fueled our query turned out to be less prevalent in this setting, in that they played a smaller role in the narratives of donors and researchers than we anticipated, in "favor" of issues we did end up focusing on; on which I elaborate in the remainder of this section.

First, the donors' narratives (as brought out in interviews), forced us to reevaluate our ideas of the structure and nature of donors' decision-making. We found that rather than this being guided by authority and deference to someone hierarchically above them (in a sense that would be detrimental to autonomy, as discussed above), central to donors' decision-making was a remarkably strong sense of *trust* – either in the form of decision-makers' trust in the researchers, or in cases of elder consent, family members' trust in their elders to promote their interests in deciding about research participation. Hence, we had to flip our beliefs regarding the autonomy in such decisions: rather than donors being limited or restricted in exercising autonomy, a more correct description of the situation seemed to be that they in fact engaged in an exercise of autonomy by actively and reflectively choosing trust to guide their decisions. In this way we came to focus on the role and nature of trust in decisions in a research context, and how it relates to exercise of autonomy. The relevance of this issue was further exacerbated by our realization that making decisions based on trust in a medical research context seems to be a universal and global phenomenon, as witnessed by the overwhelming number of studies from across the world, showing that research participants – in contrast to what is usually believed by medical ethicists – generally decide in this manner. Article 2 in this dissertation deals with this issue.

Second, experiencing the collection of samples from donors 'in the flesh' and witnessing how the informed consent process actually played out, and relating these impressions to the accounts of donors on the one hand (regarding hopes, concerns and expectations) and researchers on the other (regarding strategies for and challenges in sampling and informing), turned our attention to the stark power asymmetries in this context, with respect to knowledge, status and authority. In particular, we experienced a recurring mismatch between the interests and strategies of the researchers and the expectations of the donors, in a way that sparked the uneasy intuition that this exchange was somehow exploitative. We were thus compelled to pursue this intuition from a philosophical perspective, in order to determine whether the situation was in fact one of exploitation, and if so, exactly what factors made it so. This is the topic and errand of Article 3.

In this manner, embarking on an empirical investigation of the field forced us away from merely employing an armchair approach and settling for the issues that the literature would dictate to be ethical issues, to actively engaging with the issues that actually appeared on the ground. We thus avoided pursuing issues that may seem highly pertinent in theory, but are of less prevalence in practice. Had we stuck with our initial theoretical questions it would likely have kept the project's outlook highly cultural relativistic. This would automatically have resulted in a focus on the differences between the two cultures, and might have resulted in casting the theoretical challenges in a light that makes them look more

insurmountable than they are. This would in its nature have complicated the endeavor to come up with solutions, and if we had come up with any, their purely theoretical grounding would likely make for a poor fit with reality.[2]

[2] As I will argue, current ethical guidelines suffer from this flaw. This is not least the case with respect to the two ethical issues that we did end up focusing on, namely informed consent and exploitation.

Article overview

The present dissertation is comprised of three research articles. Article 1 details the findings of our empirical study executed in Pakistan, and Articles 2 and 3 each provide a thorough philosophical investigation of two issues that emerged as relevant in this study.

Article 1, **"I didn't have anything to decide, I wanted to help my kids" – An interview based study of consent procedures in sampling human biological material for genetic research in rural Pakistan",** details the qualitative study that has served as empirical basis for the dissertation's other two articles. This study was comprised of 10 semi-structured interviews with families who have donated blood samples to NIBGE for research on a genetic disorder in their family, and 5 semi-structured interviews with NIBGE researchers. Interviews with donors focused on their motivations to donate samples, their experience of consent and donation, and what factors were central in the decision to give consent. Interviews with researchers focused on the institute's requirements for consent, and the researchers' strategies for and experiences with obtaining consent in the field.

The study found that researchers often modify standard procedures for informed consent in the field to the local context, in order to gain the trust, good will and cooperation of the families. In turn, the donors reported that central to their participation in the research was their hope for getting something out of their participation (in the form of a cure, or knowledge about the disorder), and above all their trust in the researchers as both human beings and medical professionals as being capable and willing to look after their interests in this regards.

Noting that several of the donors may have suffered from therapeutic misconception with respect to the potential benefits they may gain from their participation, the article concludes that while trust is important in consent to research, it should be supplemented by efforts to ensure proper provision and understanding of relevant information, specifically about the nature of research *per se* (as opposed to diagnostics).

This article is co-authored with Peter Sandøe and Jesper Lassen, and has been accepted with revisions for publication in AJOB Empirical Bioethics.

Article 2, "**Is consent based on trust morally inferior to consent based on information?"** engages in the philosophical and medico-ethical discussion regarding the theoretical justifications for the practice of informed consent to medical research. In much of medical ethics it is standardly assumed and claimed that decisions based on *information* (e.g., about a medical intervention, or about the drug used in a clinical trial) are more robust and prudent than decisions based merely on *trust* (in e.g. the doctor, researcher and/or the medical institution). This attaches a superior moral value to decisions based on information, and in turn places moral weight on the information itself, as a means to reach decisions that are, ostensibly, morally superior.

In contrast to this standard claim, we argue that decisions based on trust are *not* morally inferior to decisions based on information. This argument is carried forward through a systematic analysis of the moral values underlying and essential to informed consent – i.e., autonomy, voluntariness, non-manipulation and non-exploitation – with respect to whether these values are less protected by consent based on trust than they are by consent based on information. The analysis finds that this is not the case,

and on this basis we conclude that trust-based consent is not inferior to information-based consent. The article concludes by considering and rejecting possible objections to this stance, and considers the implications this new perspective on informed consent may have for current practice, e.g. in the case of practices for ethical committees, and the practice of broad consent to genomic and biobank research.

This article is co-authored with Klemens Kappel, and has been published in Bioethics, 31(6), pp. 432-442 (DOI: 10.1111/bioe.12342).

In **Article 3, "Exploitation and vulnerabilities in biobanking in developing countries"** I explore the concept of exploitation in the context of biobanking in developing countries – thereby taking the long-standing ethical debate regarding exploitation in medical research in developing countries, and situating it in the context of biobanking, in which this issue has not yet been examined to any extensive degree.

Using the collection of and research on samples from Pakistani donors detailed in Article 1 as a case study, I examine whether this case is one of exploitation – and if so, what factors and features contribute in making it so. This is done by analyzing the case from the point of view of dominant theories of exploitation (e.g. Wilkinson 2003, Wertheimer 1996, Goodin 1987). This analysis finds the case is not one of exploitation. However, I find this result unsatisfactory, and further argue that these theories are inadequate in providing a thorough analysis of the relevant features of the case. I offer that employing a more nuanced view of what constitute vulnerabilities in exploitation and in research situations can highlight locally specific features of this case that are problematic with respect to exploitation, which may be overlooked by the dominant approaches. I conclude that this finding is applicable to cases of medical research in developing countries generally, and provide suggestions for how this may be implemented in current policy.

Background and state of the art

In the following, I account for relevant features of a) the cultural and social landscape in Pakistan, and b) the nature and practice of biobanks. I do this because these particular factual circumstances have, in ways that will be made clear over the course of the dissertation, a bearing on what ethical issues arise in this context, and how these can and should be handled on a theoretical level. Because of this interplay between practice and theory, the following factual descriptions play an important role in setting the scene for my theoretical investigation.

I then give an overview of the state of the art in the areas most pertinent to my field of inquiry; i.e. ethical issues in biobanking (in particular the idea and practice of informed consent), and research ethics in developing countries.[3] Via this account I aim to make clear how my dissertation provides important contributions in these areas and helps move the debate forward.

Pakistan

Demographics

With its population of over 200 million people spread out on an area of 796,095 square kilometers, the Islamic Republic of Pakistan is the seventh-most populous country in the world.[4] The country is divided into several provinces (Balochistan, Punjabi, Sindh, Khyber-Pakhtunkhwa) and a number of tribal areas, with local languages, traditions and customs.

22,3% of the population live below the poverty line (poverty being significantly higher in rural areas), and CIA has stated that the country "remains stuck in a low-income, low-growth trap".[5] Illiteracy is high (over 40% of the population, the third largest number in the world; with 2/3 of illiterates being women). According to UNESCO, education statistics are equally dire: over one in three young Pakistanis have not completed primary school; nearly half of young urban women from rural areas have never had the chance to go to school; and in 2010, the country allocated only 10% of government spending on education (a number that is still decreasing). This leaves a great number of the country's many inhabitants without basic skills (UNESCO 2012). For these reasons (among others), Pakistan is widely considered a developing country (Sher 2016, UN 2012).

The country is often described as characterized by a highly hierarchical structure – both in public matters, but also extending into the private sphere. There are many mentions of power structures being clearly defined along sex and age; and wisdom being attributed to age, commanding respect, loyalty and obedience (see e.g. Zaman 1992). Hence, it is often described that families accredit decision-making authority to the elder of the family, as they are considered to hold the wisdom to know what is in the best interest of members of the family and the family as a whole (Moazam 2006). Many commentators have described Pakistani society as family-centered, meaning that the family, not the individual, is the held to be the fundamental unit of society and decision-making – as articulated by Farhat Moazam,

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[3] Recently there has been criticism regarding the term 'developing countries', as it ostensibly implies inferiority with so-called developed countries, and assumes a desire to develop along the traditional Western model of economic development. Furthermore, and despite its widespread use, there is no universally and officially accepted definition of the term (Fernholz 2016). Nevertheless, a vast majority of the literature on the topic I have consulted in my research employs the term 'developing countries', so for this reason I will defend and maintain my use of this term throughout this dissertation.

[4] https://www.cia.gov/library/publications/the-world-factbook/geos/pk.html [accessed Mar 13, 2017]

[5] Ibid.

> *"The individual is viewed as sociocentrically enmeshed in inextricable social bonds, ties that make interpersonal processes the source of vital decisions ... you are your family, and your family is you" (Moazam 2000).*

This is reflected in housing arrangements, as it, especially in rural areas, is not uncommon to see several generation of the same family living under one roof, pooling their resources (Moazam & Jafarey 2005).

Research using social psychologist Geert Hofstede's model of cultural dimensions[6] supports this: on the dimension of individualism,[7] Pakistan holds a score of 14 out of 100 (compared to 74 in Denmark, and 91 in the United States), and the authors conclude that

> *"Pakistan, with a very low score of 14, is considered a collectivistic society. This is manifest in a close long-term commitment to the member 'group', be that a family, extended family, or extended relationships. […] The society fosters strong relationships where everyone takes responsibility for fellow members of their group. In collectivist societies offence leads to shame and loss of face, employer/employee relationships are perceived in moral terms (like a family link)"* ("Pakistan", n.d.)

Consanguineous marriages and genetic disorders

Consanguineous marriages (or cousin marriages; i.e. between two people with a common grandparent or other recent ancestor) are common practice in Pakistan, actively preferred by 50-60% of the population. This is mostly for social and cultural reasons, including the beliefs that such unions offer the best opportunity for compatibility between husband and wife, and between the bride and the mother-in-law; that undisclosed problems regarding health or other attributes of either bride or groom will be effectively avoided; and that it avoids sending either the bride or groom into an environment that is virtually unknown (Hussain 1999). Consanguineous marriages are more prevalent in rural areas, and among individuals who are illiterate and hold only a low education (Hussain & Bittles 1998).

This marriage practice results in an increased birth prevalence of children with severe recessive genetic disorders (e.g. thalassemia, microcephaly and muscular dystrophy). Generally, most people carry one or two variants of a gene that may cause a recessive disorder, but that is not expressed when a dominant allele is present – so, in non-consanguineous partnerships and reproduction there is only a very small chance that one's partner will have the same genes as oneself that may cause a recessive disorder. However, consanguinity increases the chance that both parents will carry any recessive variant of a diseased gene being transmitted in their family: when the partner of a carrier of a recessive variant carries an equivalent recessive variant, their children have a 25% chance of inheriting it from both parents and suffering from the corresponding disorder (Modell & Darr, 2002).

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[6] This model of national culture is based on Geert Hofstede's comprehensive study of how values in the workplace are influences by culture, and describes the values of a country by according it a score on each of six scales: Power Distance Index; Individualism vs. Collectivism; Masculinity vs. Femininity; Uncertainty Avoidance Index; Long Term Orientation vs. Short Term Orientation; and Indulgence vs. Restraint (see Hofstede, Hofstede & Minkov 2010).

[7] Designating the degree of interdependence a society maintains among its members, and its preference for either *"a loosely-knit social framework in which individuals are expected to take care of only themselves and their immediate families"*, as opposed to "*a tightly-knit framework in society in which individuals can expect their relatives or members of a particular in-group to look after them in exchange for unquestioning loyalty"*. "Dimensions of national culture", n.d.

Islam and (bio)ethics in Pakistan

95% of Pakistani citizens are Muslims, and the country's sociocultural life and values are greatly shaped and informed by Islam. Religious belief plays a central role in the life of both men and women from all social strata, and is a major influence in all public and private activities. Hence, religion and ethics are two sides of the same coin: moral authority and a sense of right and wrong are derived from religious tenets. Moral direction for action guidance is sought through the *Quran* (the central religious text of Islam) and the *Sunna* (the traditions of the Prophet Muhammad). These sources form the basis of Islamic Law, *Shari'a*, guiding all private and public conduct. If no direct answer can be acquired through the Shari'a, opinions from Muslim scholars or jurists are sought (Moazam 2000, Reinhart 1983).[8] This is the case with respect to everyday life, political activity, and, with the advent of new biotechnologies, has also been the case with bioethical issues and dilemmas (Gatrad & Sheikh, 2001) – often resulting in the issuing of a fatwa, a religious opinion about a specific new matter, according general Islamic principles and other resources such as the Quran, Sunna, consensus and analogy (Alahmad & Dierickx 2012). In this way, issues emerging in the context of medicine and biotechnology have historically and ethically been dealt with through religious thought.[9]

In contrast to this practice, the 1980s saw the advent of a 'Western-flavored' bioethics in Pakistan, led by members of the medical community that had been trained in Western institutions, and who returned to Pakistan to practice and teach. This first 'wave' of bioethics was highly focused on Tom Beauchamp & James F. Childress' paradigmatic "four principles" (autonomy, beneficence, non-maleficence, justice) as being fundamental elements to ethical codes and action (Beauchamp & Childress 2001).

However, it was eventually recognized that this approach to bioethics, originating in the secular, individualistic and rights-focused West, is an ill fit when imported to the Pakistani society – one with a different outlook on cultural and religious values, one that *"rests on a strong sense of mutual responsibilities and obligations in life, where people are comprehended as interdependent beings with different levels of power, wisdom and privilege";* which also extents to the realms of health, illness and the doctor-patient relationship (Fox & Swazey 2008). There are stark and significant differences between the lived realities of the USA and the UK, where principled, individual-focused bioethics originated, and Pakistan, where a relational morality prevails (Fox & Swazey 2008). As Moazam & Jafarey write, a *"biotechnology in Pakistan might be identical to that in the West, but it is being applied in a country with a very different epistemology of what constitutes right and wrong and how this is to be determined"* (Moazam & Jafarey 2005, p. 254). This resulted in a desire among healthcare professionals in consulting the opinions of Muslim scholars (*ulema*) on various bioethical issues, which highlighted that for a bioethical model to flourish in Pakistan, it is essential to incorporate religious and cultural sources of moral values. An important step in this direction was the establishment of the Center for Biomedical Ethics and Culture (CBEC) in the Sindh Institute for Urology and Transplantation, Karachi; an academic center for research and teaching that seeks to unite bioethical principles with local cultural and religious practice (Jafarey & Moazam 2010).

[8] This simplified account by no means gives justice to the full, intricate complexities and subtleties of Islamic law and ethics. For a detailed and illuminating discussion, see Reinhart 1983.

[9] This is evident e.g. in how relatives to terminally ill patients, as reflection of the religiously informed custom regarding decision-making on behalf of other family members, in consultation with the physician discuss how to withhold the diagnosis from the patient as an effort to spare him or her additional suffering at the end stages of life (a custom that would be viewed as highly paternalistic in Western societies) (Moazam 2000); or in the stance that termination of pregnancy is prohibited after 120 days, because that is when, according to Quranic text, ensoulment of the fetus takes place (Gatrad & Sheikh 2001).

Biobanks

Biobanks are biorepositories that store human biological samples for use in research in a vast variety of fields; e.g. epidemiology of common complex diseases, oncology, stem cell research and research on rare genetic disorders. Biobanks may be situated in a range of institutions, e.g. hospitals, universities and pharmaceutical companies, and may vary in size, methodology, composition, economy and governance (Tutton 2010).

Samples (most commonly of blood, skin or other tissue) are most often linked to genetic information about their donor. Sample donors may be individuals from a population with (a) certain disorder(s), providing material for research into that/the specific disorder(s),[10] or samples from healthy individuals for control.[11] Samples can be constituted of leftover human tissue from surgery (e.g. tumors), or human material that is actively donated from participants from a certain population of interest (usually by giving a blood sample).

Biobanking is not a new phenomenon (the systematic collection of human cells and tissues dates back to the 19th century; Gottweis & Zatloukal 2007), however, the past two decades have seen a considerable development in its use in the context of genomic research (Cambon-Thomsen, Rial-Sebbag & Knoppers 2007). Here, samples are increasingly used in genome-wide association studies, using large collections of samples to identify biomarkers for disease; in the development of personalized medicine; or to uncover the genetic basis for certain genetic disorders. Importantly, this recent surge in biobanking activity and research have showed an increased ability to and interest in linking the biological and genetic data with general information about patients/donors, as this allows for the inclusion of demographic information about donors in the study of, for example, cancer and lifestyle diseases, and in the study of genetic and environmental factors in the etiology of disease (Gottweis & Zatloukal 2007). This has largely been facilitated by the advent of large patient registries and advances in genetics, which have catapulted the ability to tap the collections of material and its potential uses.

This potential is magnified even more when biobanking goes international. There is a still-increasing international collaboration between biobanks situated in different countries, and recent decades have seen the rise of international biobanking infrastructures, e.g. BBMRI-ERIC.[12] Such collaborations often involve physical samples and their associated data being exchanged across national borders, which has a number of benefits for researchers: it provides researchers with a vastly expanded material for research that they otherwise might not have had access to; it may provide grounds for comparison from different nationalities with respect to a specific disorder; and it may easily provide researchers working on rare diseases not common in their country with material for their research.

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[10] E.g. the *Infectious Diseases Biobank* at King's College London, UK (http://www.kcl.ac.uk/lsm/research/divisions/diiid/about/facilities/biobank/index.aspx [accessed March 29 2016]), or the Mitochondrial Disease Biobank at the Mayo Clinic, USA (http://www.mayo.edu/research/centers-programs/mitochondrial-disease-biobank/overview [accessed March 29 2016])

[11] E.g. *PKU-registret* at Karolinska Universitetssjukhuset, Sweden (http://www.karolinska.se/for-vardgivare/kliniker-och-enheter-a-o/kliniker-och-enheter-a-o/karolinska-universitetslaboratoriet/cmms---centrum-for-medfodda-metabola-sjukdomar/pku-biobanken/; [accessed March 29 2016]); or *The Danish Neonatal Screening Biobank,* Denmark (http://www.ssi.dk/Diagnostik/Center%20for%20Neonatal%20Screening/Den%20Neonatale%20Screenings%20Biobank.aspx [accessed March 29 2016])

[12] http://www.bbmri-eric.eu/BBMRI-ERIC/about-us/ [accessed Mar 31 2017]

Ethical issues in biobanks

Even though human material has been systematically collected and registered since the birth of modern medicine, it is the recent growth in international exchange of samples and the increased ability to link biological and genetic information with general patient/donor information that have triggered public debate and turned academic attention to a large number of ethical issues in biobanking, both on a national and an international level. In the following I give a brief account of such issues that have been the subject of widespread ethical discussion.

First, there is the issue of *non-discrimination* (related to concerns about data security and misuse of data): since samples stored in biobanks are linked with general genetic information about its donor of potential availability to a number of researchers and affiliates, some have voiced concern that this information may be misused by e.g. employers and insurance companies to (illicitly) gather information about potential new employees' and policyholders' genetic profile and predisposition for certain disorders, and discriminate upon this information (Gottweis & Zatloukal 2007, Tutton 2010, Clayton 2003). As a means to prevent this, the Genetic Information Non-discrimination Act (GINA) was established in 2008 (Clifton et al. 2008).

The concern regarding discrimination reflects a second and broader contested issue in biobanking, namely that of *privacy and confidentiality* (Gottweis & Zatloukal 2007; Cambon-Thomsen et al 2007, Tutton 2010). By making samples and associated genetic and health data available to many researchers at once, biobanks effectively move what may have been given in a doctors' office – bound by familiar standards and obligations of the patient-doctor relationship, i.e. trust, privacy and discretion – out of this guarded, confined context and lays it open for viewing by a potentially unknown and unlimited number of people. This has caused publicly voiced discomfort, where people fear that their 'dirty underwear' will be made publicly available (see e.g. de Vries & Tomlinson, 2016). What such statements reflect is a (legitimate) desire to control what one shares with whom and be in charge of one's own narrative, as a means of exercising one's autonomy. It is largely agreed that this desire should be taken seriously; hence the debate on how to best protect donors' privacy while not delaying scientific progress is still ongoing.

The issue of *benefit-sharing* has also caused debate (Knoppers & Abdul-Rahman 2008, Vayena et al. 2008, GeneBanc 2009). In the context of research, benefit-sharing broadly refers to how profits, results, developments, technologies, treatments, and/or anything else that may be considered a beneficial outcome of a given research endeavor should (or should not) be shared among those who, in one sense or another, have contributed to the endeavor (e.g. researchers, participants, sponsors, host institutions, etc.). Benefit-sharing is debated generally within research, but has proved especially tricky to deal with in the context of biobanking: there is no direct benefit for participants, and biobank projects may only in the future (if at all) produce health or monetary benefits, which in turn may be difficult to measure and divide in an appropriate and just manner. Furthermore, since contributors to biobanks are often large populations, and most of the funds for biobank projects are currently provided from public sources, there are both logistical and theoretical challenges related to benefiting each contributor directly – as some commentators have noted, *"compensating the public at large would be equal to sending taxpayers' money back to taxpayers"* (GeneBanC 2009, p. 23). On the other hand, these considerations need to be balanced with an appropriate recognition of donors' contribution (in one form or another) so as to not discourage participation. In any case, it is still an open question (and one that is still being debated) what the appropriate nature of benefits from biobanking, and an appropriate scheme for their distribution, should be (the ongoing discussion on

'undue inducements' – i.e., the concern regarding offering benefits of such a nature and size that it distorts judgment with respect to voluntary research participation in individuals with scarce resources – is a debate of its own; see e.g. GeneBanC 2009, Ballantyne 2008, Ganguli-Mitra 2012)

Another issue causing much controversy is the notion of *property and property rights* (Tutton 2010, GeneBanC 2009): what sort of ownership do donors have over their samples once deposited in the biobank, and what sorts of rights and entitlements should follow from it? Rooted in traditional theories of self-ownership (e.g. Nozick 1974), many have the intuition that since the sample came from the donor's body, he or she has a natural ownership of it and 'the fruits of its labor'. However, this is in apparent conflict with the stance of current biobank guidelines, which argue that in order to secure the promised health benefits in the form of new diagnostics or drugs, the biobank (encompassing its researchers etc.) must have intellectual property rights over the sample and its potential offshoots. Attempts to solve such disagreements have mostly been rooted in the legal system, and case law (e.g., the case of *John Moore v. Regents of the University of California*, see Bergman 1992) has established that tissue in itself – that has not been invested with and altered by human labor – cannot be considered property). However, this strategy has proved largely unsatisfactory in addressing the concerns and intuitions of the public regarding genetic property rights. This may be because the notion of personal ownership over one's bodily material in this particular context is intimately related to a sense of privacy. As pointed out by Klaus Høyer (2008), tissue samples are sometimes viewed by potential donors as a source of genetic information about individuals that is perceived to be revealing something essential about them – which fosters a want and need to control this information in the pursuit to be the director of one's narrative; as detailed in connection with the issue of privacy above. Furthermore, it may be argued that new biotechnologies raise new problems, and it may not be adequate to try and solve them through existing law and practice. Instead, novel conceptual discussion and clarification is needed (e.g., on exactly what property means in the context of blood samples in biobanks).

Closely related to the theoretical notion of property and property rights is the practical aspect of *commercialization* (Tutton 2010; Knoppers & Abdul-Rahman 2008, Vayena et al 2008)*:* whether biobanks should be allowed to sell samples to third parties, and if so, whether and how the individual donor should benefit. Underlying and fueling this debate are also theoretical currents regarding the commodification of the human body, something that is largely viewed morally reprehensible (see e.g. Wilkinson 2003). However, this theoretical stance, if effected, vastly complicates the exchange of samples between biobanks, and may thus serve as an effective brake on the productivity and development of new diagnostics that may benefit humanity (Cambon-Thomsen et al 2007). It should be noted that this may be less problematic if what is being sold is the *data* associated with the sample, not the sample itself. But as discussed above, the current ethical and legal framework for property rights regarding sample data is inadequate with respect to fully addressing and accommodating the concerns of the public regarding their rights over their personal data. As indicated, this may partly be owed to the not yet fully developed conceptual framework regarding data and samples in the context of biobanking. The issue of commercialization remains far from resolved.

Another practical issue is that of *secondary or future use of samples* and their associated data (Cambon-Thomsen et al 2007; Knoppers & Abdul-Rahman). Since a sample, once deposited in a biobank, in principle can be stored indefinitely and may be utilized a great number of times, this allows for the sample to be use in multiple research projects and by multiple researchers – around the globe, and in the future; even after the death of its donor. Most often a sample is donated with a specific research project or

areas in mind, but general ethical guidelines in research dictate that subjects, through the practice of informed consent, should always be informed of what 'they' participate in – something that is made complex due to the nature of biobanks.

This last set of challenges point to what is arguably the most important and controversial ethical issue in the context of biobanking; namely that of *informed consent* (Cambon-Thomsen et al. 2007; Tutton 2010, Høyer 2009). This may be due to the fact that informed consent is a fundamental principle in medical ethics, but also because the issue of informed consent to research encompasses and relates to many of the issues discussed above: through the ritual of informed consent, individual donors in each case of donation (ideally) decide on contested matters such as commercialization, benefit-sharing, privacy and secondary use with respect to their sample. In the following I discuss the idea and practice of informed consent, and criticisms hereof.

Informed consent

Informed consent is an ethical cornerstone in all medical research involving humans or human material. It has gained particular prominence in the wake of historical cases of abuse of research subjects, such as the Tuskegee syphilis study (see e.g. Jones 1981) and the Nazi experiments in World War II (see e.g. Annas & Grodin 1992). In notable response to the second case, the Nuremberg Code of research ethics was established in 1949, and its very first paragraph famously states that *"The voluntary consent of the human subject is absolutely essential"* (Faden & Beauchamp 1986, p. 156). The principle and importance of individual informed consent in medical research has further been stressed and elaborated in the Declaration of Helsinki's §25-32 (World Medical Association 1964).

Informed consent is held to be an indispensable element of medical research ethics, as it allows individuals to exercise their autonomy in the form of the fundamental right to have a say in what happens to their physical being, and to decide, on adequately informed grounds, whether and how their body or body parts and associated information will be used in research. For informed consent to participation in medical research to be ethically and legally valid, participants need to be provided, at their level of comprehension, with information about the purpose, methods, demands, risks, inconveniences, discomforts and possible outcomes of the research (including likelihood and form of publication of research results), and on this basis voluntarily agree to participate in the research (Lipworth et al, 2006; Eyal 2012b). As a general rule, this information is given in writing (in informed consent forms), and the patient or research subject confers his or her acceptance and agreement via a signature.

Agreeing in this manner is, throughout much of medical ethics, held to be an expression of autonomy. Autonomy may, at the broadest level, be conceived of via its translation from Greek, *self-rule* (or *self-determination*): to rule oneself in accordance with personal wishes, preferences and aims. On this interpretation, it is possible to see how, at least on a superficial level, informed consent relates to autonomy: the patient or research subject relates the information to her wishes, preferences and aims, and on this basis decides on a course of action for herself regarding the suggestion.

However, as several commentators have noted (see e.g. Eyal 2012, O'Neill 2002), it is by no means clear exactly how we should understand the notion of autonomy in medical ethics. I will not go too far into this debate, but note one critical area of opacity; namely whether autonomy should be understood in an *instrumental* or an *intrinsic* sense. This in turn has important implications for how we should conceive of informed consent and its importance. An instrumental conception of autonomy[13] implies that since

[13] As put forth by e.g. John Stuart Mill (1859).

individuals are the best judges of what is good for them, letting them decide for themselves is an instrument to produce the best consequences for them. A defense of informed consent rooted in such a conception would typically hold that in much the same manner, giving individuals the options and means to decide for themselves in a health context produces the best consequences for their overall health. Conversely, an intrinsic conception of autonomy[14] would hold that deciding one's own course of action in itself is good for individuals and the overall quality of their lives. A defense of informed consent rooted in such a conception would typically hold that since deciding one's course of action is a good in itself in life generally, this holds in health contexts too. I go further into this discussion in Article 2.

Above these conceptual disagreements, there is widespread disagreement as to whether insisting on promoting autonomy in a health context is always the preferable strategy – in contrast, in certain situations and contexts there may in fact be good pragmatic reasons to let autonomy be overridden by other values. This becomes particularly salient in situations where individuals are sick or facing a threat to their health or livelihood, in which insisting on making them deliberate on information about the intervention that may help them is, at best, in conflict with their best interest, at worst may have unacceptable costs. As Nir Eyal notes,

> *"The cost of ensuring that one decision is absolutely autonomous may be a severe, permanent, or fatal health problem. This health problem will likely affect well-being more than a small marginal decrease of autonomy would"* (Eyal 2012, p. 8).

As such, there seems to be grounds for questioning whether autonomy is always the right, or most important, value to promote in a health context generally (and in (informed) consent specifically), and for, in turn, replacing or at least supplementing the (somewhat myopic) focus on autonomy with attention to other values. In Article 2 I defend such a view, and argue for the value of *trust* as a promising candidate.

Informed consent in biobanking

In the context of clinical research, for which informed consent was initially and primarily intended (Faden & Beauchamp 1986), the requirements for valid informed consent accounted for above are fairly straightforward to meet: in most cases of clinical research, researchers have fairly well-defined ideas about the purpose and nature of the research (as set out by their research agenda); its likely demands, risks, inconveniences and discomforts (based on experiences from earlier phases of research); the possible benefits/results hoped to be gained from the research; and in the form in which such results will be disseminated. Hence, it is relatively easy to disseminate this information to research subjects.

When applied to the biobanking context, however, informed consent becomes notoriously tricky to deal with. Given that the nature and aim of biobanks is to store samples for an indefinite duration of time, and to allow access for multiple researchers for multiple purposes, it is impossible to inform individuals – at least with the specificity required by current standards for informed consent – comprehensively about the research they (or more accurately, their sample) will participate in: since the content of future research projects cannot always be predicted at the time of sample collection, informing participants about the nature, purpose, risks, benefits and potential results of such future research uses becomes a complicated, if not impossible, task (Lipworth et al 2006; Kegley 2004).

This had led some to argue that we should abandon the idea of informed consent in biobanking (Kaye 2004), while others maintain the importance of keeping donors informed (as a means to retain public

[14] Found e.g. in objective list theories, see e.g. Parfit 1984.

trust, which is necessary to ensure continued donation; see e.g. Eyal 2012a). Attempts to accommodate the challenge of informed consent in biobanking have fostered novel and innovative schemes for consent such as *blanket consent* (which covers and allows any use of the material at any time in the future; see e.g. Kegley 2004); *broad consent* (where a donor consents to his/her sample(s) being used once at the beginning of a research experiment; and if additional analyses need to be performed or new experiments are designed, the donor isn't contacted again, provided the new research does not deviate in significant ways from what was agreed to initially; see e.g. Tutton 2001); and *dynamic consent* (where donors have the opportunity to, or are asked to, re-consent to every new experiment or any slight change in research; see e.g. Kaye et al. 2015). However, none of these models have gone uncontested.

Over the course of the last two decades the concept and practice of informed consent as a general guiding principle in medical practice and research has also been met with criticism. In the following two sections I will highlight two areas of contestation that are of relevance to my project (others include the phenomenon of 'consent fatigue' among patients; that the logistics of the documentation are procedures of obtaining re-consent are too demanding; and the charge that informed consent as a legal tool serves to protect doctors and researcher from litigations more than it protects the interests of the patient of research subject – see e.g. Eyal 2012b).

Critique of informed consent as a Western ideal

The moral notions and ideals motivating the practice of informed consent, i.e. autonomy and individuality, have their roots in Western moral philosophy and date back to the European enlightenment. One example is John Stuart Mill's famous claim that each individual knows best the way to his or her own happiness, and that for a society to flourish we ought to protect and promote the right and ability for each individual to live in accordance with his or her preferences:

> *"Each is the proper guardian of his own health, whether bodily, or mentally or spiritual. Mankind are greater gainers by suffering each other to live as seems good to themselves, than by compelling each to live as seems good to the rest […] If a person possesses any tolerable amount of common sense and experience, his own mode of laying out his existence is best, not because it is the best in itself, but because it is his own mode"* (Mill 1993 p. 81; 135).

These ideals have come to influence medical practice and inspired a move away from paternalism and a general spirit of "the doctor knows best", and established the idea of 'patient autonomy' in Western medicine: that each patient should be provided with the information and authority for him- or herself to decide on any medical course of action (Eyal 2012b).

However, they do not ring quite as true in non-Western communitarian and collective societies, which may have a different approach to weighing the preferences, actions and authority of the individual against those of the community or family. This presents challenges to the practice of informed consent (at least in its paradigmatic form, as detailed above) in such societies in medical practice and research alike; both with respect to the importance of information and that of individual decision-making.

In many non-Western countries it is not uncommon for physicians to be reluctant to give full disclosure about grave or terminal illnesses, and instead substitute ambiguous words and expressions: in Pakistan the physician is advised to delete 'frightening nomenclature' when delivering news to patients; according to one study fewer than 40% of oncologists in countries such as Japan and Africa use the word 'cancer' when talking to patients; and another study has reported on a strong Navajo cultural belief that such 'negative words' may be further detrimental to the health and welfare of patients (Moazam 2000, p. 32). Instead, it is a recurrent practice for the physician to consult with the family and mutually devise what

should be said and how it should be said, outside of the knowledge of the patient whom it concerns. This practice would no doubt quickly be dismissed as highly paternalistic in a Western doctor's office, however in the aforementioned contexts it is viewed as an act of love and care for the patient (Jafarey & Farooqui 2003; Moazam 2000), and as such generally morally laudable.[15]

This custom of collective decision-making also challenges the individualistic focus inherent in informed consent, and has resulted in complications 'on the ground' when recruiting participants for research in societies where decision-making more often revolves around collective rather than individualistic considerations of well-being (Ganguli-Mitra 2008a). As articulated by Margaret Sleeboom-Faulkner & Prasanna Kumar Patra,

> *"In certain cultures, elderly members, heads of households or heads of the community are meant to take decisions on matters that in other cultures would be considered as a transgression of personal life. Among tribal communities, decisions on health and illness are not a personal prerogative, but rather a matter to be decided upon by the religious or community leaders."* (Sleeboom-Faulkner & Patra 2012, p. 243.)

Here, obtaining consent involves engaging in and respecting often complex authority- and decision-making structures – as exemplified by Tindana et al.'s study of informed consent processes in a rural African setting:

> *"The process of consulting leaders and household heads about any new activity in the community, including research, follows a long-established protocol. […] Approaching chiefs involves paying respects to the chief and the presentation of small gifts of cola nuts and a bottle of spirit. The research is explained to the chiefs, and then permission from chiefs to conduct activities in a community is given verbally. Similarly, household heads give verbal consent to approach individuals. Only after these steps have been completed may researchers approach individuals to invite them to participate in research."* (Tindana et al. 2011, p. 2)

In such contexts, important decisions are taken as a community, not by the individuals, and for this reason the notion of individual autonomy may make little sense, and a practice of decision-making based upon it – such as paradigmatic informed consent – may be ethically questionable.

Such challenges have given rise to a substantial amount of criticism of the practice of informed consent as being highly 'Western-centric' (Kegley 2004; del Pozo & Fins 2008), in that it does not properly respect alternative community values and modes of decision-making and may potentially fail to provide adequate protection of research participants from such communities – as expressed in the following comments:

> *"Some cultures […] may make little use of the notion of individual autonomy […], at least in the sense used in research ethics, and in such cases, relying solely on individual informed consent to make it licit to carry out research may be ethically questionable"* (Ganguli-Mitra 2008a, p. 122)

[15] This should of course not be taken to mean that paternalistic acts and acts of love are in opposition – indeed, many paternalisic acts likely stem from, exactly, love and care. Take for example a mother who places the cookie jar out of reach of her son (to his dismay), so as to keep him from fulfilling his wish of devouring its entire content in one sitting (what we may have here, then, is a morally justified form of paternalism). What I intend to suggest here is that there are weighty cultural influences on how the kind of paternalistic decision-making I have detailed here is morally evaluated.

> *"[With indigenous people], informed consent as an individualist model [cannot] authorize research and the associated benefits and risks that are borne by groups* […] *Informed consent simply is an inadequate mechanism to assess and regulate the effects of research on groups"* (Burgess & Tansey 2009, p. 199-200)
>
> *"Autonomous communities have their own politics, beliefs and values and research may affect any of these elements. In a community that makes decisions collectively, merely seeking informed consent from individuals may harm the political structure."* (Weijer, 1999, p. 503)

While the endeavor to properly and genuinely respect and accommodate local cultural values and practices in research has caused voiced caution with respect to the danger of surrendering to cultural relativism (Weijer 1999), it is generally recognized that the charges in the comments above are warranted and serious with regards to the ethical legitimacy of the research enterprise in general. Hence, there have been many efforts to design and propose schemes for group or collective consent (Burgess & Tansey 2009, Sleeboom-Faulkner & Patra 2012). However, there is as of yet no general agreement on how to best accomplish this task – one that, in its nature, is further complicated by the fact that there are huge variations in cultures across the globe with respect to more norms, standards and customs for decision-making.

The roles of trust and information in consent

As indicated above, one strong theoretical justification for informed consent is that it protects and promotes individual autonomy with respect to decisions regarding research participation: when we provide prospective research participants with comprehensive information about the research, we enable them to consider this material, relate it to their personal preferences and life goals, and on this basis decide whether or not to participate in the research. On this ideal, then, necessary and sufficient requirements for autonomous decisions about research participation are a) information about the research, b) thorough consideration of this information, and c) a decision made based upon this information.

However, this theoretical ideal is in stark contrast with reality, as evidenced by the still growing number of studies (see e.g. Nobile et al. 2016, Wadmann 2013, Høyer 2010, Molyneux et al. 2005a, McDonald et al. 2008, Kass et al. 1996) showing that potential research participants more often that not do not give much consideration to the provided information about the research in deciding whether to participate or not; or, when they do consult the information, this is not a determining factor in their decision-making process. Rather, they rely on other factors as central to their decision, the all-dominant one being that of *trust*, both in the researchers as individuals, and the research institution and enterprise.[16] This is for example evident in Nobile et al.'s recent study of decision-making of German donors invited to participate in a cohort study with an attached biobank:

> *"It was observed that a trustful relation between participants and specific research institutions was determinant in the decision-making process. […] The name of the institution and the trustworthiness attached to it seemed to have acted as strong facilitators for a positive decision to enroll for a majority of participants. […] Participants further emphasized the trustful relationship they had developed toward the study over time. This trust further explained how participants did not feel the need to know the details from the*

[16] In Articles 1 and 2 I give a fuller account of the theoretical concept of trust, and the relevant distinction between *interpersonal* and *institutional* trust.

> *study, relying instead on their trust in the scientists' expertise"* (Nobile et al. 2016, pp. 2-7).

Now, it could be expected that this sort of trust-based, information-waiving decision-making in a medical context would be more prevalent in collective and hierarchical societies that imbue certain individuals, institutions and professions with distinct authority and responsibilities. Quite to the contrary, it is interesting to note that this tendency to base decisions regarding research participation on trust rather than information is observed on a global level (the countries in the aforementioned studies being, respectively, Germany, Denmark, Sweden, Kenya, Canada and the United States). Hence, it appears universal for people to rely on trust in medical settings regarding both treatment and research, even in societies that value personal and individual authority in other areas of life (O'Neill 2002). What is yet to be further investigated, but may be claimed as a plausible hypothesis, is that such tendencies are related to the special significance and nature of trust in medical relationships (in particular its relation to vulnerability) – as pointed out by several commentators:

> *"Vulnerability is primary and unavoidable in medicine, and so it is proper to think of trust arising from conditions of vulnerability. […] Because trust arises from patients' need for physicians, the greater the sense of vulnerability, the higher the potential for trust. […] The extraordinary strength of trust in physicians cannot always be justified by a calculated evaluation of objective evidence. Instead, it may arise as a coping mechanism in response to the intense psychic distress created by illness"* (Hall et al. 2001, pp. 615-617).

> *"The vulnerability associated with being ill, together with the knowledge of the medical expert spawns a need for trust in an uneven relationship of trustor (patient) and trustee (physician). […] Trust in interpersonal relationships in the healthcare settings rests on two things: competence and best interest. The trustor believes in the trustee's competence (technical skills and knowledge) and that she will understand and have the best interests of the trustor at heart"* (McDonald et al. 2008, p. 36). [17]

Such empirical findings are thought-provoking fodder for the recent theoretical debate on whether information should in fact be accorded the paramount role that it currently plays in consent procedures, and, accordingly, whether it might be time to rethink the role that trust plays in consent to medical research. Perhaps most prominently, Onora O'Neill (2002, 2004, 2007) and Neil Manson (2007) have attacked the resistance to trust in bioethics and medical practice, one that they claim is based on a conception of trust as being *"intrinsically immature, risky and unintelligent"* (Manson & O'Neill 2007, p. 159). According to the authors, this alleged sort of blind trust, combined with the bad will and/or negligence of a few researchers, has been viewed as the root of evil in cases such as Tuskegee (see above) and Havasupai (Van Assche 2013). Partly through the extraordinary attention that has been paid to the cases via both public and academic channels, this mistrust has been allowed to extend to the medical research enterprise as a whole, fostering as the most plausible and logical solution ever more thorough managerial accountability and comprehensive informed consent. As O'Neill write,

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[17] This is particularly evident in cases where patients are invited to participate in research, where it is commonly observed that *"The subject assumes the beneficient concern on the part of her physician is equally applicable to him in his role as research worker. Therefore his roles of physician and research worker and the associated qualities are conflated in the eyes of the subject"* (McDonald et al. 2008, p. 39).

> *"The story that we tell ourselves is that traditional doctor-patient and researcher-subject relationships were based on trust, that trust was often abused, and that we have dealt with the problem by ensuring that medical treatment and biomedical research do not take place without the informed consent of autonomous individuals which provides an ethically superior basis for medical practice and biomedical research."* (O'Neill 2004, p. 273)

However, the extensive procedures of disseminating information that have come to be associated with informed consent may in fact increase research subjects' suspicions and mistrust with the endeavor, rather than fostering their trust and positive attitude (O'Neill 2002). This is perhaps not surprising: wherever there is the need to document something so thoroughly, it automatically raises suspicion about its legitimacy. This becomes even more prominent in the context of medical care: in situations of need and fear, patients want competence and not having to make decisions. Being forced to consider a large amount of information often leads to frustration and distrust in the capabilities of the doctor as a caregiver (O'Neill 2002, p. 38; 48). Placing weight on patient autonomy, majorly conceived of as the right and responsibility of the individual patient to accept or refuse care, *"may encourage ethically questionable forms of individualism and self-expression and may heighten rather than reduce public mistrust in medicine, science and biotechnology"* (O'Neill 2002, p. 73).

Instead, Manson and O'Neill have advocated bringing back *trust* as a guiding normative principle between in the relation between researcher and subject (or between doctor and patient);[18] observing that trust is an indispensible element in all human relations, not least within the medical context, and one that cannot be replaced by ever-growing systems of accountability and documentation such as informed consent (Manson & O'Neill 2007, p. 158). The authors recognize that trust in doctors and researchers (as in people of all others professions) can indeed be mistaken should they turn out to be untrustworthy (which can have grave consequences both for the individuals involved, for the public attitude and for society as a whole), however, the authors find it mistaken to believe that the problem of (un)trustworthiness *"can be improved by establishing robust and transparent systems of accountability in all areas of life"* (ibid. p. 159). Increased documentation will perhaps prevent certain instances of misconduct; however will not increase trust, but rather erode the relation between truster and trustee. Consider an analogy: it is possible that we might be able to prevent infidelities in romantic relations by issuing contracts prohibiting such behavior, making it mandatory for any couple to sign it before entering into a romantic union, and actively punishing breaches of this contract. However, it seems intuitive that entering into such an ostensibly necessary contract would only serve to make lovers acutely aware and suspicious of their partners' propensity to cheat, something they might not have considered before. Furthermore it is likely that their awareness of the probability of this treachery on part of their partner, as manifested by the necessity of the contract, will pervade their future relation and make the foundation of it one of suspicion, instead of trust – which stands in stark contrast to how we, generally, wish the nature of our romantic relationships to be. Moreover, and contrastingly, it seems that there can indeed exist faithful romantic relations without the existence of enforcing contracts.

I take these considerations to be descriptive of Manson & O'Neill's view of trust relations generally, i.e., we can have functioning relations based on trust which do not need documentation or sanctions for them to be robust and functioning. In contrast to others theorists, they maintain that this nature of trust relations do not, as a rule, lead to abuses of trust in the medical context. To the contrary,

> *"Relations of trust may sometimes offer a more realistic basis for medical and research practice if – but only if – reasonable evidence to support the placing or refusal of trust is available. If medical and research practice can be anchored in trustworthy structures and*

[18] This stance is supported by other theorists, see e.g. Miller & Weijer 2009.

> *practices, which offer reasonable evidence of their trustworthiness, they may earn others' trust, while untrustworthy structures and practices may fail to do so"* (Manson & O'Neill 2007, p. 159).

Hence, placing trust intelligently in the medical context does pose requirements, i.e., sound structures and practices on which individuals may base their trust. But this is a claim much different from the wholesale exclusion of the role of trust from decision-making in medical research; a move that, according to the empirical studies mentioned above, fits poorly with reality. On my reading of Manson & O'Neill, their errand is a wish to "re-recognize" the intimate and personal nature of the relation between researcher and subject, one that essentially one of trust, and take this as a starting point for designing mechanisms for accountability and oversight in medical research institutions and practice.

In Article 2 we challenge the established institution and practice of informed consent with considerations of this sort (although not leaning extensively on the accounts of Manson & O'Neill), and advocate how and why it is defensible to rely on trust in consent to medical research, rather than on information. This article thus contributes to the current debate on the justification and validity of informed consent in general, with particular focus on the proper roles on trust and information in consent. Furthermore it offers theoretically well-founded suggestions for future policymaking in this area.

Research ethics in developing countries

All the ethical issues in the context of biobanking that have been discussed up to this point are further exacerbated in an international context by the fact that, for the time being, there exist no internationally binding ethical guidelines for biobanks (Cambon-Thomsen et al 2007, Gottweis & Zatloukal 2007), meaning that each country may have their own responses to the ethical issues laid out above, which makes for shaky grounds for their accommodation. This is not least the case when developing countries – often characterized by poor infrastructure and instable political environments – are involved in international biobanking.

As such, these challenges detailed above obtain when moved to the developing world context; however here there are additional issues that can challenge the ethical legitimacy of any medical research being conducted in this context. These circumstances have spawned much debate on the ethics of conducting medical research in developing countries, especially when this is carried out by researchers based in a developed country.

In the following I will highlight two areas of this debate that are of particular importance and pertinence to my project, namely the practical challenges in obtaining proper informed consent (and the ethical obligations that this fosters), and the concern regarding exploitation in medical research in developing countries.

Practical challenges in obtaining proper informed consent

Let us for a moment set aside the internal theoretical problems that haunt the notion and practice of informed consent (as discussed above), and focus on the monumental role it, after all, does play in actual medical research ethics. From this point of view, there is a vast amount of literature reporting on the practical difficulties in properly informing potential research participants (as a prerequisite for obtaining proper informed consent) in developing countries (Benatar 2002, Choksi et al. 2007, Molyneux 2005a, 2005b). These sources most commonly cite illiteracy, linguistic barriers, and lack of education as factors that serve as obstacles to the process of informing potential research participants.

Given that information about the research is commonly offered in written forms, and the acceptance of this is commonly given through a signature, this quite naturally poses challenges in obtaining informed consent from individuals who are illiterate. Solutions to this problem have been offered in the forms of verbal consent, proxy consent (where a literate acquaintance or relative signs on behalf of the consenting individual; having a literate acquaintance read aloud to the consenting individual, and/or having the consenting individual providing a fingerprint instead of a signature). However, studies indicate that in spite of these measures the consenting individuals ultimately often do not have much idea of exactly what they have consented to; i.e. the nature and aims of the research and how it might affect them (Sleeboom-Faulkner & Patra 2012; Afolabi et al. 2014). Another challenge to the practice of written consent is that it is not uncommon for individuals in certain societies or communities in developing countries to be suspicious of providing signatures or fingerprints, as a result of prior experience with exploitation by local landowners and others, after putting their formal agreement on something they did not understand (Sleeboom-Faulkner & Patra, 2012). In addition to these challenges, the languages of some cultures and tribes in developing countries may not have appropriate corresponding words for some of the scientific terms that are needed to convey relevant information about the research to potential participants (examples could be "gene" or "placebo"), which may compromise comprehension. This is exacerbated by the generally lower level of higher education in many developing countries, meaning that many individuals will not have had the chance to acquire familiarity with scientific jargon and practices, including the nature of research (Nyika 2009; Hawkins & Emanuel 2008).

It has, however, been questioned whether lack of literacy, exact translations of scientific terms and higher education is really necessary to reach a level of comprehension that is adequate for being able to consent on properly informed grounds (Nyika 2009). For instance, it can be argued that you do not have to understand to exact nature of a gene to be able to understand, that the genetic research one participates in involves investigating what has been passed down to you from your mother and father, respectively. Moreover, it is by no means an impossible task to work out information procedures that convey the relevant information regarding the nature, risks and benefits of the research in a manner tailored to the cultural and linguistic framework of specific communities. Suggestions for this involve having investigators fluent in local languages serving as a safeguard to ensure accurate translation, and the collaboration between researchers and linguists in 'word creation', involving relating a concept like "gene" to attributes of heredity already understood in the local language (Choksi et al. 2007).

While the claim that one does not need to know exact details of something to agree it does seem right (e.g., I can agree to going out for a coffee without knowing beforehand at which coffeehouse, or from where they source their beans), it is still worthwhile to note the prevalence of *therapeutic misconception* in the context of developing countries. Therapeutic misconception *"occurs when a research subject fails to appreciate the distinction between the imperatives of clinical research and of ordinary treatment, and therefore inaccurately attributes therapeutic intent to research procedures"* (Lidz & Appelbaum, 2002, p. V-57) – i.e., when a research subject conflates research participation with diagnostics/clinical care, and mistakenly believe they will receive personal health benefits from their participation. In the context of developing countries, therapeutic misconception is often partly ascribed to a lack of education, resulting in a lack of familiarity with the difference between research and treatment and their respective goals (Macklin 2003, Benatar 2002). It does not seem far-fetched to claim that lack of familiarity with the nature of research does in fact have an impact on the susceptibility to therapeutic misconception. However it is worthwhile to note that the phenomenon is also commonly observed in developed countries and with educated populations (Wadmann 2013, Appelbaum et al. 1982, Kass et al. 1996), hence it cannot fully be explained with reference to a lack of education.

Exploitation and vulnerability

Exploitation of research subjects in medical research has been an ongoing debate for some time, and this concern is only magnified in the context of developing countries (Macklin 2003; Hawkins & Emanuel 2008; Crouch & Arras 1998, Annas & Grodin 1988). Here, commentators have voiced concern regarding the scenario where researchers based in wealthy, developed countries conduct medical research on individual in poorer, developing countries. Here, the issues most commonly causing concern are

1) The problem of *benefit-sharing* (see Ganguli-Mitra 2008b, 2012; Sleeboom-Faulkner & Patra, 2008): that there are no mechanisms in place for ensuring that whatever results that accrue from the research will be shared with the people or community that participated in research, to properly match the risks and harms they might have endured in their participation, or
2) The problem of *reasonable availability* (see Hawkins & Emanuel 2008): that the products, interventions, treatment or technology for which the research is used will either not be of relevance to the population being used as subjects, or will be outside their scope of what they can afford.

The shared intuition in these concerns is that either amounts to *exploitation* of the research participants,[19] because the researchers, sponsors and/or people in the developed country where the research is institutionally based will benefit far more than the research participants (and often the research participants take on substantial risks through participation, e.g. in the form of severe drug side effects).

What makes the charge of exploitation in medical research particularly serious in developing countries is that here the potential research subjects are often already in a bad position (given common ills in this context such as poverty and lack of access to medical care), and exploiting them in the ways detailed above will make them even worse off, which amount to a grave injustice. A common school of thought here is that due to the abovementioned ills, individuals here will be even harder pressed to accept any offer of medical care – even placebo trials where they might not get anything out of their participation, or experimental drug trials where they might risk grave side effects – without much thought to potential bad consequences (Kamuya et al. 2014; Hawkins & Emanuel 2008). As such, individuals in developing countries are often held to be *vulnerable* in medical research, in the sense that due to their dire circumstances they are more likely to accept research proposals that may not serve their best interests or those of their community. Many historical cases of research conducted in developing countries do indeed point to the plausibility of this interpretation, such as the Surfaxin Trial conducted in Bolivia in 2000:

> A private U.S. drug company tested Surfaxin, their drug for alleviating respiratory distress syndrome, a potentially fatal disease, on 650 premature infants at risk of dying from the disease. Surfactant therapy has been approved for use in Latin America, however its high cost makes it a non-viable option for most infants in the country. Furthermore, the principal target market for Surfaxin was the U.S. and Europe, and the sponsor had no specific plans of marketing the drug in Latin America. The infants in the Surfaxin trial were given endotracheal ventilator support with either Surfaxin or a placebo drug. The ventilator treatment in itself, including either of the treatments, was known to improve general survival and was thus better than the treatments generally available to both groups prior to the study. Hence, parents agreeing for the infants participate would have good reasons to do so, even though they might not be able to afford the drug down the line, or knowing that their neighbors would not (see Hawkins & Emanuel 2008, pp. 58-61).

[19] I give a thorough discussion of the theoretical concept of exploitation in Article 3.

Responding to cases such as this, ethical guidelines for medical research go to great lengths in identifying *groups* that may be vulnerable and for whom special protections should be in place. Many of such guidelines point to individuals in developing countries as fitting candidates for this description (see e.g. CIOMS 2002, U. S. National Commission 1979, WMA 1964). However, many commentators have recently pointed out that these guidelines are mistaken in conceiving of vulnerabilities in virtue of group membership, i.e., in this case equating being from a developing country with being vulnerable. What this approach overlooks is that vulnerability is not a constant, but is rather highly contextual – as Tea Logar articulates it, *"people are not vulnerable simpliciter, but are usually vulnerable only to some people, and only in certain respects"* (Logar 2009, p. 335).

I believe this approach is correct, however, the literature representing it (see e.g. Kipnis 2001; Liberto 2004; Luna 2003, Logar 2009) is still lacking in conceptual clarity. In particular, it (to a bigger or smaller extent) fails to make clear what exactly the nature vulnerability is, and in turn how it makes one open to exploitation. What I take these contributions to suggest is that we should conceive of vulnerability as entailing a locally specific impairment of one's ability to reason and make decisions (contrary to this being a constant, as abovementioned guidelines would offer), which makes one more open than normally to accepting transactions that do not serve one's best interests (I pursue this line of thought in Article 3). As such this is yet uncharted territory, and I believe it would be beneficial to refine these theories' insights regarding the subtleties and contextuality of vulnerability into a criterion of exploitation.

The ethical issues that arise in medical research in developing countries have most commonly been discussed in the context of clinical research, e.g. randomized controlled trials and placebo studies of new drugs or technologies, and to a lesser extent in the context of biobanking. This is particularly true with respect to the issue of exploitation: as of yet, there exist hardly any studies or discussions of this issue in the context of biobanking in developing countries. Hence, Article 3 in this dissertation constitutes an important contribution in filling this gap in the debate on exploitation in medical research in developing countries. In addition, it responds to some of the internal shortcomings in the theoretical groundwork in this area, in that it offers a refined view of what constitutes vulnerability in potentially exploitative situations (both in a research context and otherwise), and when and why vulnerabilities become a problem – the latter being a question the answer to which is necessary to develop policies and practices that appropriately and adequately accommodate them. Hence, this article contributes to debates in both medical research ethics and practice and in philosophical theory.

3. Methodology

As stated above, this project was comprised of 1) a qualitative interview study and 2) philosophical analyses based upon its findings. In the following I account for the respective methods and strategies employed in these two parts of the project (I go into further technical and formal details regarding the qualitative study in Article 1).

Qualitative interview study with biobank donors and genetic researchers (Article 1)

The aim of the interview study detailed in Article 1 was to investigate and explore the experiences, considerations and decision-making strategies among NIBGE donors regarding their donation and participation in research.

The setup of the qualitative interview study was established in the conception of the *Global Genes, Local Concerns* project framework: 10 semi-structured interviews (of a duration of approximately one hour) with donor families, recruited by NIBGE from their database of donors according to the following criteria: individuals from rural areas, living in a traditional family system, with low levels of income, education and literacy.

In preparation for the interview study, I conducted an extensive literature review focusing on a) ethical issues in international biobanking and genetic research (with particular focus on developing countries and hierarchical societies), and b) the landscape for medical and bioethical decision-making in a Pakistani context, on both political and individual/family levels. Based on this review I found the issues most pertinent for further investigation to be those of *informed consent* and *decision-making* in this context (what factors are central in donors' decision to consent; how does the consent process work in practice; what sort of and extent of information about the research do donors have available; how are authoritative relations negotiated), and *benefit-sharing/future uses of samples* (what do donors expect to get in return for the participation, if anything; how do donors feel about their samples being used for genetic research on others than 'their' disorder; what are their considerations regarding property of the sample).

These issues informed the development of the interview guide (see Appendix 1), which I carried out in collaboration with Klemens Kappel, Peter Sandøe, Julie Zahle and Klaus Høyer. During the literature review I identified two Pakistani scholars in bioethics, Farhat Moazam & Aamir Jafarey of the Centre for Biomedical Ethics and Culture (CBEC) in Karachi, who were very kind to provide helpful input to the interview guide from a 'local' point of view. Prior to traveling to Pakistan, I conducted a number of pilot tests of the interview guide with individuals of Pakistani origin residing in Denmark, and adjusted it accordingly.

At NIBGE, donor informants were brought to the institute for their interview with us. In all cases, several family members were present at interviews, with the father or both parents doing most of the talking. Since all informants spoke little or no English, the interviews were conducted with the assistance of an interpreter, who translated our questions from English into either Urdu or Punjabi (according to the language informants felt most comfortable speaking) and the respondents' answers into English. Besides the informants, the interpreter, and myself, an observer from the GGLC project was present at interviews. Interviews were recorded (with informants' permission), and during the interviews the observer and I took notes on how informants' statements did or did not align with the theoretical framework we had set out beforehand, and other emerging conceptual and ethical issues of potential value to pursue further.

After each interview, the interpreter, the observer and myself held a debriefing session to discuss the interview: what were the salient considerations and issues of this family, did anything come up that we had not considered previously, and how could we pursue these issues in the next interview? We also used these sessions to refine the articulation and ordering of certain questions, for improved understanding and response from the informants.

While conducting interviews with donors, several issues emerged on which I would like the opinions and experiences of the NIBGE researchers. In parallel with donor interviews, I thus set up interviews with the researchers who had the most extensive experience in collection blood samples from donors for research (5 researchers in total). The interview guide for these sessions (see Appendix 2) was thus developed 'on the go', and informed by the questions and issues that caught my attention during donor interviews. There were mainly related to the researchers' experiences with the sampling process; the institute's requirements for consent; and how and why the researchers adapt conventional consent requirements to their specific local context.

For donor interviews, I transcribed the English portions (i.e., my questions and the donors' responses as translated by the interpreter) verbatim. For interviews with researchers, I did verbatim transcription of sections found to be most relevant to the issues these interviews were meant to explore.

Transcriptions of both sets of interviews were coded and analyzed using the software package NVivo. I used codes corresponding to conceptual areas of interest to highlight donors' and researchers' statements regarding these issues. Some of these had retained from our original interview design (e.g. autonomy; informed consent); some had emerged as prominent themes during the process of conducting donors interview (e.g. trust and its different forms; different forms of authority/deference).

This systematic process of coding and analysis of donors' and researchers' accounts and considerations served to highlight central and relevant conceptual themes, to be subject for further philosophical analysis. Without claiming any sort of expertise in the field, I would venture that this hybrid empirical-philosophical approach can be seen as a variant of the method of *grounded theory* – defined by Strauss & Corbin (1994) as

> "*a general methodology for developing theory that is grounded in data systematically gathered and analyzed. Theory evolves during actual research, and it does this through continuous interplay between analysis and data collection"* (Glaser & Strauss 1994, p. 273).

I say "a variant of grounded theory" because the way in which I apply this approach is not with the aim of analyzing data in order to generate new theories, but rather in the further development and modification of existing philosophical ones. In any case, would I argue that this still offers the benefits of a grounded theory approach, namely that (as I also indicate in the Introduction),

> *"Theory derived from data is more likely to resemble the "reality" than is theory derived by putting together a series of concepts based on experience or solely through speculation (how one thinks things ought to work). Grounded theories, because they are drawn from data, are likely to offer insight, enhance understanding, and provide meaningful guide to action"* (Strauss & Corbin 1998, p. 12).

A few reflections on the validity of my interview data are in order. First, certain factors may call into question the sincerity of donor responses. Recalling the general norm of elder authority, this may have had an effect on the response of some individuals – e.g., not wanting to say something that may displease

their elder (typically their husband/father), or that defies or questions his authority, when he was in the room. Furthermore, a great majority of informants expressed gratitude for the fact that NIBGE had contacted them and offered their assistance. Even though I made clear that I was not working for NIBGE, and that what was said in the room would not be relayed to researchers, it can be speculated that some informants still did not want to risk saying something that would jeopardize their relation to the institute and, in effect, the potential benefits they might accrue from this relation.

Second, it is worth considering whether researchers (either consciously or not) responded to my questions probing their experiences and strategies according to a certain agenda. For example, as I detail in Article 1, NIBGE researchers often have to balance formal requirements for informed consent with local customs, sometimes slacking the formal procedure in order to secure cooperation (in the form of sample donation) from families. As formal informed consent from donors is a requirement for publishing their research results in international journals, NIBGE researchers may have had an interest in obscuring how often this breach of international standards takes place in the field, and conversely to demonstrate their general willingness and efforts to comply with formal standards and requirements.

Philosophical strategies of inquiry (Articles 2 & 3)

Articles 2 & 3 employ two well-known instruments from the toolbox of analytical philosophy: *conceptual analysis* and *reflective equilibrium,* and Article 3 furthermore makes use of a *case study.* In the following I give a short introduction to these methods, and give examples of how I employ them in this dissertation.

According to Frank Jackson (1998), the role of conceptual analysis is "*to make explicit our 'folk theory' about a given matter, elucidating our concepts by considering how individuals classify possibilities"* (paraphrased in Beaney 2003). Conceptual analysis entails subjecting our (everyday) notions and concept to systematic scrutiny, most commonly by breaking them down into their constituent parts, in order to gain a clearer understanding of the situation or issue in which they are involved. Conceptual analysis can be very useful in making sense of our (sometimes fuzzy) intuitions and claims about the world and the nature of phenomena in it, and determine which should and should not be grounds for political decision- and policy-making. Conceptual analysis has in particular proved helpful in the fields of public health ethics and bioethics, in elucidating e.g. the nature of *responsibility* in claims such as "individuals are responsible for their own obesity" and the value of *naturalness* in claims such as "we ought not to engage in human cloning, because it is unnatural".

In Article 2 we argue that the values inherent in informed consent – autonomy, voluntariness, non-manipulation and non-exploitation – can be upheld to a similar or larger degree by trust-based consent. In order to make this claim, we employ conceptual analysis of all the theoretical concepts involved in this claim – information, consent, autonomy, voluntariness, manipulation, exploitation, and trust – in that we break them down into their constituents, to determine what they stand for. This deconstruction allows us to see if we can piece back together the puzzle in a way that fits the claim 'trust-based consent is not morally inferior to informed consent'.

Similarly, in Article 3 I set out to investigate whether the collection of blood samples for biobanking in rural Pakistan is one of exploitation. To determine this, I first need to determine what 'exploitation' is. With the aid of the literature on exploitation, I break this concept down into its constituents and end up with conceptual puzzle pieces such as 'unfairness', 'benefits', 'moral duty not to take advantage' and 'vulnerability' (this list is illustrative, not exhaustive) – all of which in turn call for another round of analysis, to determine what *they* refer to. Only upon completion of this, I can then work my way backwards to a more thoroughly defined concept of exploitation, which can be used as a measuring stick to answer whether my case is exploitative.

Following John Rawls and Norman Daniels, *reflective equilibrium* consists in working back and forth between our judgments or intuitions about particular situations or cases, and our moral principles and other relevant background theories;[20] and revising either of these elements as needed in order to achieve an acceptable coherence among them. When we succeed in this, we have achieved reflective equilibrium. The method can be used as a tool for testing and choosing between contrasting intuitions, actions or practices: we should choose the one that most convincingly can achieve coherence with our other principles and intuitions (Rawls 1993, Daniels 1979).

Article 2 can be seen as an exercise in reaching reflective equilibrium between our intuition "trust is as good as information in consent" and the standard claim in the literature that "consent based on information is better than consent based on trust". In order to accomplish this, we find that it is necessary to revise the standard claim and its background intuitions (in which conceptual analysis is helpful, as explained above), which ultimately leads to its refutation.

In Article 3 I analyze the Pakistan case from the point of view of different exploitation theories, with the aim of determining whether it is exploitative on any of these accounts. Their general answer is that it is not. However, I do not find this answer satisfactory, as my intuition still tells me that the case is exploitative. I must then attempt to achieve equilibrium among my intuition and my moral principles (in this case, the theories of exploitation). I can either discard my intuition, or revise my moral principles. I choose the latter, and engage in a revision of the notion of the element of *vulnerability* in exploitation. This revised and refined concept of exploitation allows me to articulate a sense in which the case is exploitative, and I thus achieve reflective equilibrium between my intuition and my theoretical framework.

Furthermore, Article 3 employs the method of a *case study*. Case studies as a tool are less common in analytic philosophy in comparison with the two above, thus there is less background material and justification to its name. Case study analysis within the discipline of philosophy has been defined as *"a method of describing a situation that is representative of an issue such that the issue, the stakeholders, the decision makers, relevant factual information, alternative solutions, and core values are made clear in detailed written form"* ("How to Think About Philosophical Issues" [course notes], n.d.), highlighting its inherent philosophical values, issues and dilemmas for involved stakeholders (and in some cases society at large), which may then be subject to further philosophical analysis and discussion.

In the conclusion of this dissertation (which follows after the articles) I discuss how empirical approaches, such as case studies, and philosophical methods may valuably complement each other.

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[20] Following Norman Daniels (1979), we may distinguish between *narrow* and *wide* reflective equilibrium. Narrow reflective equilibrium is limited to seeking coherence between particular cases and moral principles, whereas wide reflective equilibrium includes other (non-moral) background theories.

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Article 1: "I didn't have anything to decide, I wanted to help my kids" – An interview based study of consent procedures in sampling human biological material for genetic research in rural Pakistan

This article is co-authored by Jesper Lassen and Peter Sandøe, and is has been accepted with revision for publication in AJOB Empirical Bioethics.

Abstract

Background**:** Individual, comprehensive and written informed consent is broadly considered an ethical obligation in research involving sampling of human material. In developing countries, however, local circumstances such as widespread illiteracy, low education, and hierarchical social structures complicate adherence to these standards. Consequently, researchers in such settings may modify the consent procedure to local circumstances to secure participation. To ethically assess such modified consent strategies, it is necessary to investigate to which extent practices are in accordance with the values underlying informed consent.

Methods**:** Over a two-week period in April 2014, we conducted semi-structured interviews with researchers from a genetic research institute in rural Pakistan, and with families who had given blood samples for their research. Interviews with researchers focused on the institute's requirements for consent, and the researchers' strategies for and experiences with obtaining consent in the field. Interviews with donors focused on their motivations to donate samples, their experience of consent and donation, and what factors were central in the decision to give consent.

Results**:** Researchers often reported modifying consent procedures to the local context: standardly employing oral and elder consent, and tailoring the information to the social education level of specific donor family. Central themes in donors' accounts were the hope of getting something out of their participation, and their remarkably high level of trust in the researchers, as conducive to their decision to consent. Several donor accounts indicated a conflation of participation with diagnostic purposes, resulting in a therapeutic misconception.

Conclusions**:** We argue that while building and maintaining trusting relationships in research is important – not least in developing countries – strategies that serve this endeavor should be supplemented by efforts to ensure proper provision and understanding of relevant information, specifically about the nature of research, as well as measures for individual consent and opt-out.

Keywords**:** Pakistan, Trust, Informed consent, Developing countries, Qualitative research, Research ethics

1. Introduction

Informed consent has long been viewed as the ethical seal of approval for any medical research project involving human subjects (Faden & Beauchamp 1986, Manson & O'Neill 2007). Paradigmatically, informed consent is constituted by the provision of written information relevant to participation in the study (duration, methods, potential benefits/side-effects/risks) together with the subject's signature, confirming his or her agreement to participate in the study (Parvizi 2008, Resnik 2008).

However, several studies reporting from research settings in developing countries (del Pozo & Fins 2008; Jafarey & Farooqui 2005, Molyneux et al. 2005a;2005b, Patra & Sleeboom-Faulkner 2012, Tindana 2006) have demonstrated the difficulties in adhering to this standard model in obtaining consent from potential research subjects. Numerous factors contribute to this, including illiteracy, lack of education, suspicion at being asked to provide a signature, and traditional communitarian and/or patriarchal family systems that problematize individual consent. Therefore, researchers have turned to alternative models when seeking to obtain consent, such as oral consent or collective/elder consent; or they have lowered standards governing the level of information required.

Some hold that this is potentially ethically problematic (LaFraniere et al. 2000, Macklin 2003, Nyika 2009). Others argue that although alternative consent procedures may not follow the requirements of informed consent to the letter, they respect the values underlying the practice of informed consent (Bhutta 2004, Fins & del Pozo 2011, Geller et al. 2004, Packer, 2011).

Given the importance of this debate, there is surprisingly little research exploring whether, and to what extent, alternative consent procedures are in practice underpinned by the values of informed consent, i.e. respect for individual autonomy, non-coercion, and non-exploitation (Beauchamp & Childress 1985, Kleinig 2004). If the debate is to move forward, more knowledge is needed of what the alternative procedures look like in practice. Hence, in this paper we present the results of a case study of the procedures for obtaining and giving consent to participation in genetic research in rural Pakistan. Our aim is to provide an overview of how alternative procedures for obtaining consent from potential research participants play out in the field.

We collaborated with a local institute for genetic research. Within the institute's Human Molecular Genetics Laboratory, researchers investigate the molecular basis of infectious, genetic and metabolic disorders, and conduct disease gene identification for various phenotypes. Sample material for this research is collected primarily from affected families living in villages in the surrounding area. Due to the local tradition of consanguineous marriage in these rural areas, there is an increased incidence of genetic disorders; hence these inbred families represent a powerful resource for genetic linkage analysis and the identification of gene mutations. Families are often very large, and families with affected children often have multiple children in the hope of having normal ones. Most adults in these families have little to no education, and there is a high degree of illiteracy. Most families have a very low income, with one or both family heads working on daily labor. Thus, many families are left in a desperate situation of having very limited resources to care for their several affected children.

Large parts of rural Pakistan are characterized by hierarchical systems in both the private and public spheres. The society is family-centered, and it is not uncommon to see several generations living together under the same roof (Moazam & Jafarey 2005). This is due to longstanding cultural traditions and religious beliefs that take the family to be the central moral unit, setting out clearly defined power structures within the family unit (Moazam 2000). This is further evidenced by the fact that authority for decision-making – regarding e.g. selection of spouse, financial actions, and also medical intervention – often lies with other family members besides the individual(s) whom the decision concerns. Thus *"personal identity takes second place to the collective family identity and consciousness"* (Moazam 2000, p. 30). In other words, individual decision-making authority gives way to the collective and/or the elder. Hence, it is not uncommon for women to have decisions made for them by their husband or their father, or for family elders to decide on behalf of their entire family.

Our study was guided by the following research questions:

1) How are formal requirements for informed consent negotiated and adapted to local circumstances, and why?
2) What factors are central to donors in the decision to consent to give blood samples for genetic research?

2. Methods

This study was based on qualitative semi-structured interviews with 10 donor families and with 5 researchers. This interview method captures informants' personal experiences with a phenomenon as told through their own words and considerations, and allow pursuing a theoretical agenda while allowing other relevant issues to come forth in conversation (Brinkmann & Tanggaard 2010, pp. 31-38). Interviews were carried out on location at the collaborating institute over a two-week period in April 2014 by the lead author. In combination, the two data sources were expected to give a nuanced picture of the multiple factors at play in the complex process of obtaining consent in this particular context, and of how they are handled and negotiated.

2.1. Interviews with donor families

We conducted semi-structured interviews with the heads of donor families (in all cases accompanied by several family members) from the rural areas surrounding the institute. The guide for donor interviews was developed based on studies of the literature targeting salient ethical issues and challenges in genetic research and biobanking, with a specific focus on developing countries and hierarchical societies. The interview questions explored how respondents had consented to giving a sample to the institute; what information they had received and whether they had employed this in their decision to give a sample; the respondents' relation to the researchers and the institute; and what factors had been central in their decision to give a sample. We received feedback on the interview guide from Pakistani researchers with a relevant background who had no affiliation to the collaborating institute. The interview guide underwent a number of pilot tests with individuals of Pakistani origin residing in Denmark and was adjusted accordingly.

The recruitment of donor respondents was facilitated with the help of researchers at the institute in accordance with our criteria: individuals from rural areas and living in a traditional family system and with low levels of income, education and literacy. Respondents were recruited from the institute's database of families who had given samples for research. Most of the families approached agreed to participate in the interviews; those that declined did so due to ongoing family functions or deaths in the family. The fact that the selection of donors to be invited to participate was left to the discretion of researchers at the institute was a source of bias: those donors that accepted the invitation to participate in interviews may have been primarily those who felt that they had a good relationship and had had good experiences with the institute. While we were aware of this potential bias, the circumstances of recruitment made it unavoidable.

Within the previous year, all of the interviewed donor family members had donated blood samples to the institute for the purposes of research into the genetic disorder afflicting one or more children in the family. The disorders were: microcephaly, icthyosis, deafness and muteness, blindness, neuromuscular dystrophy, and epilepsy. All respondents met our demographic criteria. Despite their low levels of education, a few respondents demonstrated a basic understanding of genetics (in rationalizing the

hereditary patterns of their children's disorder), and a minority offered statements indicating that they had a concept of research, as distinct from diagnosis or treatment.

Respondents were picked up from their village home, driven to the institute for the interview, and transported back afterwards. As participation in the interview – including transportation to and from the institute – meant respondents having to forego a day's labor, they were reimbursed by the amount that they would usually have earned during the lost day. Respondents did not receive any additional payment for participating in the interview.

Since all respondents spoke little or no English, the interviews were conducted with the assistance of a translator, who translated our questions from English into either Urdu or Punjabi (according to the language informants felt most comfortable speaking) and the respondents' answers into English. The translations were transcribed verbatim. To verify and validate them, recordings of interviews were subsequently checked by another English/Urdu translator, with no affiliation to the present study.

Respondents' answers were coded using NVivo. The coding was both focused/concept-controlled (guided by our themes of interest, such as consent process, relations to the institute, and decision-making) and open/data-controlled (allowing the inclusion of other emerging or recurring themes in respondents' accounts (Kvale & Brinkmann 2009, pp. 224-225)). The coding and data analysis were carried out by the lead author in close consultation with the co-authors.

Prior to interviews, respondents were informed about the purpose and nature of the study: that we, the foreign researchers, were interested in hearing about their experiences and thoughts in relation to the process of donating their sample; that the interview would last about an hour, would be recorded, transcribed and anonymized; and that they were free to break off the interview or to refrain from answering any particular questions. Acceptance of and oral agreement to this were sought from all respondents and recorded before beginning the interview. After the interviews, respondents were asked if they had any questions for the interviewer, whether they would like to add anything that our questions had not explored, and how they had experienced participation in the interview.

In the Results section, donor respondents are identified by the code given to them by the institute when taking their blood samples, consisting of an abbreviation of their disorder and a unique number.

2.2. Interviews with researchers

At the same time as the interviews with donor families, and into a short period after this, interviews with 5 researchers at the institute (2 PhD students; 2 postdocs; 1 senior researcher) were carried out. These interviews aimed to provide insights into the researchers' experiences with the sampling process; the institute's requirements for consent; and how and why the researchers adapt conventional consent requirements to their specific local context. The respondents selected here were those with the most extensive experience of sampling donors. The interview guide was developed in tandem with the process of interviewing donor families and was informed by questions and issues that caught our attention during donor interviews.

Interviews were conducted in English. Respondents were informed about the nature of the interview, that the interview would be recorded, and that it would be anonymized subsequently. Consent was sought prior to the interview and was included in the recording.

Sections of the interviews found to be most relevant, and to further our investigative aims, were transcribed verbatim, and coded and analyzed in NVivo.

2.3. Ethical approval

The study was approved by the collaborating institute's Research Ethics Committee (Jan 2014), and retrospectively by the newly established Research Ethics Committee at The Faculty of Humanities, University of Copenhagen (Sep 2016).

3. Results

We begin by presenting the researchers' accounts of the institute's consent requirements, and their strategies for, and experiences with, collecting samples and obtaining consent. We then describe the donors' accounts of their experience and interactions with the institute (including their consent to blood sampling procedures).

3.1. Researcher interviews

3.1.1. Consent requirements

The consent requirements for any study based at the institute depend on the specifics of the study. Any principal investigator must provide the institute's Research Ethics Committee with a certificate showing what questions will be put to donors and what type of consent will be employed. In most cases collective consent is used, which is a procedure where one person (usually the elder) consents on behalf of the entire family. Due to challenges posed by the high degree of illiteracy and suspicion about signing documents in the areas of operation, verbal consent is standardly used. According to the collaborating institute's Research Ethics Committee, verbal consent is "worth" as much as written consent. Written consent is rare. However, in cases where it is necessary to secure it, a literate relative or acquaintance of the donor normally reads the informed consent document aloud to him or her, thereby validating what is in the document, and where possible the researcher obtains a thumbprint from the individual donor in place of a signature. When the researchers plan on publishing study results in international journals, or on publishing results regarding one specific family, or when researchers wish to document the effects of a genetic disorder by showing pictures of donors in their publications, individual and written consent is always sought. This is most often obtained by re-contacting the family in question, explaining the situation, and taking the necessary steps to obtain individual written consent.

Consent to research participation is broad, allowing researchers to conduct various other types of research using their sample if it becomes necessary to do so, and to share the sample and associated information with other researchers – provided, at least, that this does not reveal the donors' identity or compromise the donor's privacy in any other way.

3.1.2. Strategies for sampling and obtaining consent

Researchers employ one of two strategies in recruiting donors. One is to drive to rural areas and ask around for families with children affected with genetic disorders of interest to the researchers. When families are found, the researchers then engage in a process of convincing the donors to give blood samples to the institute. In these cases, there is no previous personal relation between the donor and the researcher. Another, more utilized strategy is for the researchers themselves to either contact families from their own village or hometown who are known to have children with the relevant genetic disorders and ask for blood samples, or to ask their families and friends there for the addresses of potential donors of interest. As a group, the researchers know people all over the country who can act as reference persons, and who can recruit donors from these areas. Once a family has been identified, a team of researchers

visits them to draw pedigrees and collect samples, accompanied by the acquaintance in question. This serves both to ensure the cooperation and participation of the family and to make them feel comfortable and secure in giving their consent to participation:

> *"I will know the family, they will know me; it will be [a]… social binding that, I will do this, I will cause them no harm. […] It's consent based on trust based on the personal relation they have with me."* (Researcher 2)

In both strategies, the researchers first reach out to the elder of the family to raise their recruitment needs, honoring the local custom that the elder functions as the guardian of the family and its interests, and has authority to make decisions on behalf of the family. Consent is only formally valid with the elder's agreement, and only if the elder agrees do the researchers take samples from the family. In some cases, the researchers will also talk to individual family members about their participation, but only after consulting with the elder. Individual family members in general comply with the elder's decision that they should give samples.

When they are approaching a family, it is important that researchers quickly gain the trust of the family. In cases where researchers have no ties with the family, this is done using a case-to-case approach in which the locality of the family, their social status, and their literacy level are taken into consideration when determining how to best approach the family – how to talk to them, what information to give, and what type of consent to seek. This assessment is often made on the spot, based upon the researchers' first interaction with the family:

> *"When you enter any area, and when you visit a particular family, by saying a few greeting words, you can come to know [a lot], what is their literacy level and what type of consent we'll get."* (Researcher 1)

In all cases, the strategy of traveling to the specific family's home is the first step in earning that family's trust:

> *"The general practitioners… the patient has to go* there*; [to] the hospitals, the doctors, the clinic… When our team goes to* their *home, it is the first step to developing the trust of the family. They trust [you because] you have traveled all the way to them, just to talk to them, and to work on their disease, and you're not charging anything."* (Researcher 1)

When meeting a family, researchers begin by presenting a general introduction to their institute, explaining that they are from a government institute, and that they carry out genetic analyses to find out what causes certain disorders. Inquiries are then made about the family's structure – about who is married to whom, the family relations of the person being addressed, and how many children are affected. Gradually the researchers disclose that the children are affected because the parents are carriers for the genetic disorder in question, and the researchers may be able to help by working on the disorder and finding out more about underlying causes. The disclosure is carried out in a manner that is sensitive to the family's educational level (i.e. explaining about genes and DNA in terms that do not presuppose higher education), customs, cultural values and traditions. As an example of the latter, many families have for several generations engaged in the practice of cousin marriages, and may not take kindly to being told that what they are doing is wrong (in the sense of inadvisable). Here, researchers make an effort to be polite and indirect, e.g. by using the example of someone else: *"If he had married someone else, the condition could have been prevented"* (Researcher 1). Out of respect for the family, and to preserve their good will, researchers *"try not to use any hard words, such as 'disease''* (Researcher 1). The researchers then encourage the family to give samples, and in most cases they are successful in this. Researchers make an effort to explain to donors that the work takes a long time, and that any results may take many months or years to be derived and shared. An emphasis is placed on the fact that there is no cure for the

disorder, but that research may help to prevent the disorder arising in future generations. Donors are informed that some of the research will be done in Pakistan, but also that their samples may also be sent abroad where there is more advanced technology and expertise. The researchers view this entire process as constituting the donors' consent.

As the rural areas of Pakistan are highly divided into clans/regions with distinct and differing customs, practices and beliefs, researchers employ sensitivity to these in order to gain the trust and cooperation of families. When researchers are visiting high-risk areas of the country for sampling (e.g. conflict zones such as rural areas of Khyber Pakhtunkhwa, where Pakistani polio workers have been killed by locals as a result of suspicion of their collaboration with the CIA (McGirk 2015)), they bring someone into the team who knows the area and the people there, and can vouch for the institute. By involving a local person who knows the area and its inhabitants the researchers are able to reassure and convince donors *"[…] in their [own] style"* (Researcher 3). Researchers thereby respect local customs and practices which might have been an obstacle to the donors' willingness to participate had the researchers approached the family as strangers.

3.1.3. Challenges in obtaining informed consent

Respondents reported several difficulties in meeting the standard requirements of informed consent. Firstly, even getting donors to grasp the importance of informed consent is not always straightforward:

> *"The majority of donors have no idea that they have to give any type of consent. They suppose that once we're there, we can take their sample. Only if they say no, we will not. They have no idea that there is such a thing as [informed] consent, and that is essential. … For them [formal] consent does not matter, it only matters that they can say yes or no"* (Researcher 1).

Secondly, respondents felt there were challenges in informing donors properly and fully, e.g. in telling donors that their samples may be used in research to benefit people other than their family:

> *"When we ask them so many questions, when we share so much information with them, then they become a little reserved, and sometimes suspicious that – why are we asking so many questions?"* (Researcher 1)

Informing donors about the nature of research as such (to safeguard against therapeutic misconception) has proved especially difficult, owing to the fact that very few donors have a working concept of research and what it does/does not entail. Although researchers felt that they spent a lot of time and effort conveying the message that there is no cure for the donors' children's condition, and that any results from their samples will take a long time to derive, donors often perceived diagnostic purposes:

> *"[Many] families identify it with what you do when you have a disease; you go to the doctor, you have your x-rays taken, you have your urine sample analyzed, you have your blood sample analyzed… most people think that they are giving their sample to be analyzed for a cure"* (Researcher 4).

In other words, donors expect from the researchers what one would expect from a doctor, i.e. a cure or a treatment. When this outcome is not delivered, donors sometimes become impatient, annoyed and frustrated with the institute, contacting the researchers repeatedly for results, or breaking off cooperation entirely.

3.2. Donor interviews

3.2.1. Motivations for consenting to give a sample

One motivation to consent, salient in respondents' accounts, was the hope of gaining a personal benefit from their research participation. A majority of respondents indicated that the prospect of finding a cure for their children's disorder was central to their decision to give blood samples to the researchers:

> *"I didn't have anything to decide, I wanted to help [my] kids. [The researchers] said they'll be taking the samples and maybe they'll find a cure. ... I think that maybe in 10 days, 15 days, 6 months, a year, they maybe find a cure, so we said that's ok"* (ICT-9).

Several respondents linked this motivation to the fact that they had very limited means to care for their (often many) affected children, and were in some cases forced to work to earn a basic income instead of caring for their children at home – a dilemma causing a high level of distress for the family, as expressed by one informant:

> *"We have a very small place to live, just a small room, and we make gol gappas [popular street snack in Pakistan], and we have made a shade outside our room… the kids, all day they sit there, and… I cannot take time off from work because that will [place a] financial burden on us. […] I pray to God, either end their life or cure them"* (MCP-168).

Some respondents – those who had previously been informed of their disorders' heredity by their doctor, and who had a basic understanding of genetics – expressed suspicion that their children's condition was connected to the consanguinity of the parents; they wanted genetic counseling on whether they should break with local tradition and marry their healthy children outside of the family to protect future generations:

> *"Three of our children are normal, and they will be marrying their children [to others], so we want to know [whether] this problem persists in the next generation or not. […] Even if [they have] healthy children… will their progeny be safe or not? […] I'm a cousin of my husband […] and this problem is in my family. So that is why I'm concerned. And, the doctor says that, maybe it's because of the cousin marriage. […] Normally in the villages it is not customary to marry outside the family. So, now, that is also my concern, that I want to get rid of the problem, so I want to marry them outside of the family. To safeguard future generations"* (MCP-168).

When asked about the prospect of their samples being used in other projects or research, some respondents made references to a general obligation in Islam to contribute to the wellbeing of humanity, and the belief that those who do so will be blessed:

> *"I'll be happy if my children find a cure, or, if my children do not find a cure, maybe you could be able to find something else, or, maybe you'll be able to control another disease, in future generations, or in any other area... […] There is this thing in Islam, that is Sadka. And Sadka means giving something to someone else and doing a favor to someone. So I'll think that it's sort of that… it'll be a favor that'll be continuing for generations and generations. So I'll be happy to do that."* (NMD-28)

3.2.2. Decision-making process

Almost all respondents expressed a very positive attitude, with no hesitation, toward giving blood samples to the researchers and saw the decision to participate as an easy one. This was based on: a) it

seemed a minor sacrifice, b) it might benefit the family, and c) it would do so without any obvious risks – as evidenced by the following exchange:

> *Respondent: "So [the researchers] went [to us] and they said that they might be able to help, so what's the big deal in giving a sample of blood. So I said fine, we'll be giving it."*
>
> *Interviewer: "Okay. So you decided for the entire family?"*
>
> *Respondent: "There was nothing to decide about it, because we thought if there is no harm for our family, it's ok. […] We didn't discuss it, they've come, and I say, ok, just give the samples, and we all gave the samples"* (ICT-9).

Almost no respondents reported asking the researchers any questions about what would happen to their sample. The only concern voiced was the suspicion that their blood would be sold to third parties, but this was usually remedied by their own rationalization that such small amounts of blood cannot realistically be sold.

Many respondents said that the relationship they felt they had with the researchers was conducive to their decision to consent to give samples:

> *"I feel very good about [the researchers who came to take samples]. There were very good people; they are very good people. They just came to us just like family, just like brothers, just like sisters, and he took the girl into his lap and all that and he comforted us, and they were very friendly and very nice."* (NMD-28).

In many cases, however, this trusting relationship and attitude to the researchers was developed after the donors had received some sort of external approval that the researchers and the institute were to be trusted. This was most often the case when the family had been recruited through a friend, family member or acquaintance associated with the institute – as the parents of one family explained:

> *Interviewer: "So you told me that when the [researchers] came out, you were kind of scared, but then they just asked you for a sample. So how did you decide to give samples?"*
>
> *Respondent A: "One of the persons who was with them was from the same village that we belong to. So he also told us that it's ok, they just take the samples, […] they might be able to help you. So that's how we decided we should [do it].*
>
> *Respondent B: "[Institute employee], we know him and then he convinced us that there is nothing else, they will just use your samples for cure purposes, and you do not have to worry about anything, they are trustworthy. So that's how we trusted them"* (MCP-167).

Another trust factor was the belief that the researchers were doctors, as integrity and credibility were associated with this profession:

> *"I do not think that a doctor would do anything bad. We know that he'll be using it for research purposes. […] I firmly believe that a doctor saves lives. He does not take life. He does not do anything bad. I believe that. And if my samples are to be used for anybody else's help, or if the doctors do use them to help somebody else or cure somebody else, or do some other research, I have no issues, because I strongly trust that doctors, it is a very noble profession, and I know that doctors will respect that"* (DEM-87).

Similarly, others reported that their trust in, and positive attitude toward, the researchers was due to the fact that the researchers were from a government institute:

> *"Since it's a government institute, so, there are different projects that the government initiates for poor people, so we had this perception that this is a government institute, they'd be*

helping us" (SKD-39).

In a few cases the social custom of elder authority appeared central to respondents' decision-making:

> *Interviewer: "But how did you agree to do it – when they took your samples, did they say, I'm gonna take your sample, and you said yes, or how was it?"*
>
> *Respondent: "Since [institute employee] is, he's both of our… he's our uncle. He's [my wife's] uncle and my uncle also. And he has the status of the kids' grandfather. So we do not… he told us to give the sample, and we said yes, we give. Since he is our elder, he can decide for us. So maybe if there is a consent letter, maybe he would have signed it or something."* (NMD-28)

4. Discussion

Our study of the institute's recruitment and consent process shows a highly complex relation between formal consent requirements, social conventions and practices, and locally specific donor motivations and decision-making strategies.

Researchers at the institute tailor the consent procedure to local circumstances and customs, employing oral rather than written consent, allowing family elders to consent on behalf of their families, and adapting the level and nature of information to the background and education of the individual family. Their approach employs a high degree of sensitivity to each individual family's background, needs and customs. By making the approach to families through someone from the local area, or someone known to the family, the researchers establish contact with families in a way that will quickly make them feel comfortable and secure, and often serves to endorse the institute and its activities through the reference person and their affiliation to the institute. Furthermore, providing a person who knows the family and their background – either through a personal relationship or by being from the same locality – to recruit and inform in accordance with local traditions and customs heightens the likelihood that the family will receive information that is specifically relevant and important to them. It also helps to ensure that the information is conveyed in a manner that can be understood – it is more effective than a process in which donors are approached by someone unknown to them and/or receive the amount of information about the research that is standardly contained in informed consent documents; generally couched in technical/scientific language. Moreover, it is likely that by recruiting participants through someone they know and feel comfortable around, the researchers safeguard against the coercion and exploitation of vulnerable research subjects.

The institute's methods of obtaining consent do not comply with the standard model of informed consent, however. So in the following, we discuss whether, and how, the institute's practices respect the *values* underlying informed consent, focusing on where these values appear to be challenged by local practices.

4.1. Factors in donors' decision-making: hope for cure, obedience to authority

The vast majority of donor respondents described the consent process as very comfortable and free of any pressure from researchers, and indicated that they had the necessary information and freedom to decline or agree to participate in the research. At the same time, however, it appeared that several quite powerful factors served to shape their motivation to consent to give samples to the institute. Firstly, one overarching motivation was the hope of a cure for their children's disorders, in some cases made especially urgent by the family's dire financial situation. In these cases, the prospect of some relief from their burden appeared to be a strong driver of the donors' consent. Secondly, several respondents'

accounts indicated obedience to authority as central to their decision to consent. This was evident in the respect researchers enjoyed from being associated with the medical profession and/or being from a government institution. Obedience to authority also figured in the case of elder consent: social customs dictate that a family elder has decision-making power on behalf of his family, and our interviews indicated that an elder's decision to allow collection of samples from his family is rarely questioned, let alone opposed.

That these particular factors figure prominently in donors' accounts would appear to call into question the genuine autonomy of the decision to consent – one of the key values in informed consent. The autonomy of vulnerable research subjects' decisions to participate in medical research is an important ethical issue, and has been discussed at length in work on the coercion and exploitation of research subjects in developing countries (Gbadegesin & Wendler 2006, Hawkins & Emanuel 2008, Macklin 2003, Resnik 2003). Nevertheless, it is worth noting that, in developing and developed countries alike, consent to research participation is often induced, in part, by deference and hopes rather like those detailed above. Numerous studies show that even in contexts where laborious procedures for informed consent are in place, research subjects still base their decision on other matters, e.g. their confidence in the merits of science and doctors, their family's opinion, and their hope for results or a cure (Behrendt et al. 2010, Busby 2004, Høyer, 2003).

4.2. The social importance and relevance of trust, and its role in consent

The accounts of donor respondents generally displayed a remarkably strong sense of trust in the researchers, with this trust being cited as an overall motivating factor in decisions to consent to give their blood samples. Some respondents referred to the fact that the institute is a government institution, and as such is to be trusted. Others referred to their belief that the researchers were doctors, a belief which automatically elicited a strong sense of trust in them. It is a common notion in Pakistan that those who choose to be a doctor are necessarily good people, and this helps to make the medical profession one of the most respected occupations in the country. This respect may be further explained by the Islamic belief that the doctor is an instrument of God:

> *"[R]everence and respect toward physicians is due not only to their knowledge and scientific expertise, but also to the historical position accorded the art and science of medicine in Islam. The privileged position of physicians is derived through a historical understanding of the healer as an instrument of divine mercy"* (Moazam 2000, p. 31).

Building their trust on their general conceptions of institutions and doctors, the donor respondents displayed what has been termed *institutional trust* (Hawley 2012), i.e. trust in someone or something because they or it represents a certain institution in society. This type of trust is usually grounded in certain standards associated with the institution in question (e.g. that some professions require many years of education and specialization, or, as above, that a doctor is necessarily a good person). It may also be characterized as what Becker (1996) terms *abstract trust*: trust in something because it represents a certain type of thing or category. Although institutional trust relates primarily to an institution or category, and not specific members of it, it is not uncommon for it to "spill over" into trust in individual members of that institution or category (McDonald 2008). This may be what is happening when respondents express trust in individual researchers because they are from a government institution or the medical profession.

Other donor respondents cited the researchers' approach and conduct as factors that made them feel comfortable and reassured them that the researchers were to be trusted. This form of trust, which concerns the individuals with whom we interact, has been termed *interpersonal trust*. A key feature of it is the

truster's belief that the trustee has the truster's best interests at heart, and will accordingly act in ways that properly respect these interests (Hall et al. 2001, Hardin 2002, Hawley 2012). Interpersonal trust is often effectively established, promoted and bolstered by the behavior and personal characteristics of the trustee. As several studies have shown, this often happens in medical settings, where trust-facilitating factors include whether the doctor/researcher is perceived as compassionate and caring (Hall et al. 2001), whether, in the patients' experience, doctors do something "extra" for them in addition to following standard procedures (McDonald et al. 2008), and the patients' sense that the doctor is genuinely acting in their interests (Goudge & Gilson 2005). In our interviews donors repeatedly mentioned trust-facilitating behaviors – e.g. referring to the fact that the researchers had spoken to and treated them in a comforting and familial way, and had traveled a long distance to see them.

Donor respondents who had been recruited through a personal link explicitly emphasized this relation as central to their decision to consent to give samples. This form of *indirect trust*, and its role in driving decisions, has received less attention in the literature than institutional and interpersonal trust. However, in the case of the Pakistani donors it appeared to be as strong a motivating force as the other two, more discussed forms. To appreciate the role of indirect trust in donors' decision-making, it is necessary to understand its social and normative significance in the particular cultural context with which we were dealing. Both donors' and researchers' accounts indicated that certain expectations and obligations similar to those characterizing the bonds between close friends were inherent in the trust relationship that is forged between the researcher and the donor family via their contact person – an example would be the expectation that both will personally make sure that the other is not harmed, and that both will personally do what they can to protect and promote the others' interests.

The introduction of formal consent recorded in writing into this trusting relation could disrupt the highly valued, implicit pact of trust between donor and researcher. Moreover, in this context verbal agreements and the obligations that implicitly follow from them are regarded every bit as morally strong and binding as any signed document. The practice of quickly establishing strong indirect trust in this fashion, and of employing this trust in decision-making, is not uncommon in cultures like the one we investigated. As Farhat Moazam notes, referencing anthropologist Arthur Kleinman, in societies such as Pakistan individuals are viewed as *"sociocentrically enmeshed in inextricable social bonds, ties that make interpersonal processes the source of vital decisions"* (Moazam 2000, p. 29).

In their studies of consent practices in Doha, Pablo R. Del Pozo & Joseph J. Fins (del Pozo & Fins 2008, Fins & del Pozo 2011) have observed similar tendencies. They note that in informed consent procedures what carries the required information to the recipient is not *what* is said, but rather *who* is saying it and *where*, *when*, and *how* it is said; and they remark that there are

> *"[o]ther means of information exchange outside the customary vectors of doctor-patient communication. […] Information is being shared obliquely through intermediaries […] and non-verbal clues that are culturally specific. These side channels of communication complement direct doctor-patient communication and become part of the message"* (del Pozo & Fins 2008, pp. 273-276).

According to anthropologist Edward T. Hall this tendency to receive important messages by taking cues from the surroundings rather than relying on explicit communication is characteristic of *high-context societies*, as opposed to *low-context* ones. The contrast is explained by Geert Hofstede:

> *"[a] high-context communication is one in which little has to be said or written because most of the information is either in the physical environment or supposed to be known by the persons involved […] This type of communication is frequent in collectivist cultures*

> *[…]A low-context communication is one in which the mass of information is vested in the explicit code, which is typical for individualist cultures."* (Hofstede 2005, p. 89)

Hofstede's description of high-context societies closely resembles the landscape of communication exchange between donors and researchers in our study, indicating that what appeared, at first glance, to be gaping information holes may not have been so:

> *"[In high-context countries], people neither expect nor demand very detailed explanations, because most of the information is either in the physical environment or internalized in the person. When the bulk of information is conveyed by such implicit understandings, the explicit component of the message can be minimized without compromising the conveyance of information"* (del Pozo & Fins 2008, p. 275).

Examples of this from our case can be the government license plates on the institute's vehicle, and the fact that the researchers came a long way, in so doing conveying something about themselves and their aims. This gives weight to the general attitude among donors that they had all the information they needed, and it would also appear to make less serious the possible charge against the institute's model that it leaves out relevant and important information. Furthermore, these results resonate with findings from around the world indicating that it is very common for potential participants in medical research to base their decision to participate on trust in the researcher or medical professional, rather than on information about the research (Kass et al. 1996, McDonald et al. 2008, Nobile et al. 2016, Wadmann 2013).

4.3. Therapeutic misconception

Several donor respondents said that a motivation in giving their samples was to find a cure for their children. They later voiced frustration and annoyance that no therapeutic interventions were offered. They reported that they had been informed by researchers that their sample would be used to "check for the reason for the disease" but seemed to identify this with diagnostic purposes. This is known as *therapeutic misconception*: a phenomenon, observed in medical research with patients, in which patient-participants believe that the research will benefit them and their medical condition directly, often in the form of treatment (Appelbaum et al. 1987, Bhutta 2004, Nyika 2009). This could suggest that they have not been properly informed about the *research* nature of their participation. Note, however, that therapeutic misconception is a common challenge in medical research globally and is closely related to trust-relations in the present setting (de Melo-Martín & Ho 2007, Johnsson 2013).

In the work carried out by the institute we studied it is difficult to avoid therapeutic misconception. Owing to the general lack of education in these rural areas, not many individuals have been familiarized with the concept and nature of research, as something distinct from diagnostics and/or treatment. Further complicating the matter, and supporting the donors' assumption that they *will* eventually receive something from their participation, is the Islamic notion that every disease or ailment has a cure, and that it is the duty of the devout to strive and search for it (Pathan 2009). Thus, although researchers go to some length to inform donors that they should not expect to get anything out of their involvement in the research, it can be speculated that many donors – more or less consciously – still view their participation as a step on the way to a cure. Preventing therapeutic misconception in this setting is cannot merely be a matter of informing donors more fully about the nature of the research they are participating in, as many donors lack the proper framework for processing this information in the first place.

4.4. Limitations of the study

The donors who participated in interviews were those that already had good experiences with the institute. This may have left out the perspectives of those that had felt disenfranchised (as hinted by researchers, many donors feel let down). These perspectives could certainly be explored further, in order to shed light on possible connections between the donors' generally high level of trust and the incidence of therapeutic misconception: it might be speculated that the donors' trust in the researchers, and in their intentions and ability to help, blinds them to the information about the research that is actually provided, causing feelings of disappointment and frustration later on. However, the present study setting did not permit us to pursue these matters further.

5. Conclusion

Our study showed that while the institute's procedures for obtaining consent to research participation may be at odds with the conventional model of informed consent, researchers nonetheless seek to respect the values underlying that model – most importantly, by being sensitive to the background and needs of individual donor families, and by creating and maintaining trust. There is little doubt that trust is of considerable importance and value in good research practice, not least with participants in developing countries.

Nonetheless, in the case of research participation trust should always be complemented by the provision *and* understanding of important details of the research to be undertaken, including the nature of research itself, and the difference between it and treatment or diagnostics. One problematic consequence associated with the researchers' approach is that of therapeutic misconception: donors expressed expectations of treatment that were not met by the researchers. It appears, however, that this is difficult to safeguard against in the institute's work: it seems that the researchers do what they can to inform participants, but that as a result of their limited education and unfamiliarity with the research process donors lack the appropriate framework to comprehend the information. However, it can be argued that greater efforts might be made here, and we encourage the development of improved guidelines on informing donors in a manner tailored to their level of education, that still convey all relevant aspects.

Similarly, it would not be impossible to combine the standard practice of elder consent with individual consent – e.g. by consulting individual family members about the research after obtaining consent to participation from the elder. This would honor the local social norm of elder authority while giving individuals the opportunity to opt out.

We found that donor respondents based their consent on a number of features of their situation, and on the high degree of trust they placed in the researchers. Generally, if donors' circumstances are such that they have no viable option but to agree to participate in research, this is an obvious ethical problem. However, we did not find the situation of the respondents in our study to be so. Furthermore, numerous studies have shown that more often than not, research participants base their consent on a number of factors related to their situation, and not only on information about the study. It is recognized that in many regions of the world trust generally plays a much more significant role than information in a decision-making and consent to participation in medical research. Thus, contrary to what some accounts of the importance of informed consent claim, it may not be controversial to base consent on trust rather than information. However, trust can always be abused, and it is not, and should not be, the only relevant parameter in evaluating consent practices: in addition to maintaining a robust and friendly relation between the researcher and the research participant, it is necessary to ensure that vital information about the study is explicated and understood, and not left "between the lines". Further research efforts are needed to elucidate how this may be achieved in practice.

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Article 2: Is consent based on trust morally inferior to consent based on information?

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Abstract

Informed consent is considered by many to be a moral imperative in medical research. However, it is increasingly acknowledged that in many actual instances of consent to participation in medical research, participants do not employ the provided information in their decision to consent, but rather con- sent based on the trust they hold in the researcher or research enterprise. In this article we explore whether trust-based consent is morally inferior to information-based consent. We analyze the moral values essential to valid consent – autonomy, voluntariness, non-manipulation, and non-exploitation – and assess whether these values are less protected and promoted by consent based on trust than they are by consent based on information. We find that this is not the case, and thus conclude that trust-based consent if not morally inferior to information-based consent.

1. Introduction

Informed consent is often considered a moral imperative in medical research. Adequate and appropriate information about the study in question is a prerequisite for medical research on human subjects to be ethically legitimate. However, it is increasingly acknowledged that research subjects often do not understand the information they are provided with yet still consent, and that there is a broad array of instances in which comprehensive dissemination of information is not an option so that researchers must rely on other factors in obtaining consent. This has led some to argue that information is not paramount in actual instances of consent to participation in medical research (Walker 2013), and several recent studies (Dawson & Kass 2005, Goudge & Gilson 2005, Kass et al. 1996, Wadmann 2013) have found that reliance on *trust* rather than *information* in decision-making about participation in medical research is a common phenomenon.

This raises an important and somewhat neglected question: Is consent based on trust morally inferior to consent based on information? In this paper we argue that this is not the case: under appropriate conditions, trust-based consent is not morally inferior to informed consent.[21]

Before moving further, we would like to add two qualifications to our analysis. First, our analysis presumes that the researcher or institution that a person trusts is in fact trustworthy, and our claim is thus that in a context where the person or institution is to be trusted, trust-based consent is not morally inferior to information-based consent. We recognize that of course this, unfortunately, may not always be the case in reality – but whether the person or institution is in fact trustworthy is a different question that the one we address. We will discuss this point in more detail in the Objections. Second, our analysis concerns the relation between researcher and research subject, but it seems natural that it extends to the general

[21] The general role of trust in consent has been discussed before; one prominent contributor to this debate is Onora O'Neill (see e.g. O'Neill 2002). O'Neill's main claim (or at least one of them) in this important work is that the conception of individual autonomy dominant in much bioethics, and the theoretical justification for informed consent derived from it, is misguided; serving to undermine trust and fostering mistrust. By contrast, our more minimalistic claim is that decisions based on trust are not morally inferior to decisions based on information given the right sort of circumstances, as they may be no less prudent and can in fact be an instantiation of autonomy. To our knowledge no one has yet analyzed this particular question.

medical context (such as the relation between doctor and patient). However, we will not discuss the matter of the application to this context in the present paper.

Building on existing work on trust, we will begin by sketching an account of trust in medical settings. We will then rehearse the standard requirements for informed consent to be considered valid, namely that it must result from autonomous decision-making, be voluntary, be non-manipulated, and be non-exploitative (Nielsen 2010, Kleinig 2004, Faden & Beauchamp 1986). In the subsequent analysis, which constitutes our main argument, we assess each of the four requirements of informed consent so as to determine whether consent based on trust can make good on these underlying concerns. We will argue that this is the case. Based on the assumption that when two practices realize the same underlying moral concerns to the same degree, one cannot be morally inferior to the other, we conclude that consent based on trust is not morally inferior to consent based on information. Finally, we consider certain objections to this view, and determine that none of these ultimately pose a threat to our conclusion.

2. Trust

In the philosophical literature there is no consensus as to just what constitutes trust. However, most accounts and definitions do share common themes. As articulated by Hall et al., the majority of accounts stress "… the optimistic acceptance of a vulnerable situation in which the truster believes the trustee will care for the truster's interests" (Hall et al. 2004, p. 615). In their respectively influential accounts, Annette Baier (1986) and Katherine Hawley (2014) emphasize that trust amounts to more than mere reliance, such as when I rely on my chair not to collapse beneath me. Trust differs from mere reliance in that the truster in some sense holds the trustee accountable in case she fails to do what she is expected to do. Trust is thus 'richer' than reliance in that it has a normative dimension. This explains why violation of trust usually results in indignation and moral outrage, as opposed to mere disappointment. If I trust you to look after a precious glass vase, I am right to feel betrayed and outraged if you carelessly break it. However, it would not be appropriate to direct these normatively laden feelings towards a shelf holding the vase, should the shelf collapse and break the treasured object.

Now, it has long been recognized that trust plays a central role in medical relationships, and that certain features are unique to trust in medical settings (Goudge & Gilson 2005, Hall et al. 2001, McDonald et al. 2008). Consequently, this demands certain qualifications of the generalized account of trust above. Firstly, the literature referred to above primarily concerns interpersonal trust, i.e. trust between individuals. In a medical context, however, with a diversity of players on the field including hospitals, pharmaceutical companies, biobanks, and the medical profession at large, the phenomenon of institutional trust (i.e. trust in institutions rather than individuals) seems poignantly relevant. Furthermore, it is commonly observed and recognized that institutional trust plays a major role in recruitment for medical research: consent decisions in this context rely not just on the person taking consent, but also in the research enterprise or institution they represent (this may be a specific research center, or the medical profession in general) (Hall et al. 2001, Molyneux et al. 2005).

Secondly, and in a similar vein, the account above does not (explicitly) consider the potentially stark asymmetries that may abound in the relationship between the truster and the trustee within a medical context, such that while the researcher has expert knowledge of and insight into the study, the research subject is likely to lack a comparable understanding. Some have thus suggested that what is perceived as trust in this context, may in fact be an expression of respect for medical authority and/or an acceptance of epistemic superiority.

While these are all important questions, we can set them aside for the discussion that follows. We view our conclusions regarding the moral value of decisions based on trust as independent of these specific questions regarding various species of trust.

3. Forms of consent

In the literature on the topic of informed consent it seems to have been assumed that when potential research subjects are provided with information about the study, they actually base their decision on precisely this information. However, the numerous studies mentioned at the outset of this paper disproves this assumption: being *informed*, in the sense of being provided with relevant information, does not imply that this information is what serves as grounds for the decision made. We may then rightly distinguish between *informed consent* and *information-based consent, where informed consent refers to consent in situations where information has been provided, and information-based consent refers to consent based on information.* This difference is not widely recognized: on a closer reading, many discussants of informed consent seem to employ an interpretation of informed consent as information-based consent; taking "informed consent" to mean "consenting on the basis of information".

Building on these considerations, we distinguish between two paradigmatic forms of consent in medical research settings: information-based consent and trust-based consent.

> *Information-based consent.* A subject gives information-based consent to participation in medical research when her consent is (primarily) based on her processing of specific information about the proposed research.
>
> *Trust-based consent.* A subject gives trust-based consent to participation in medical research when her consent is (primarily) based on her trust in the requesting agent, rather than on specific information about the proposed research project.

Both are forms of consent, but they differ with respect to the roles that trust and information play. Before moving further, we should note the following points regarding the distinction drawn above.

First, consent to medical research can be based on trust rather than information when no information is provided or available, or when information is available but the consenter is not interested, or again when information has been understood by the consenter, yet the content of the information plays no significant role in her decision to consent while trust does.

Second, it seems likely that in many (if not all) actual cases, consent will be based partly on trust, and partly on information. So, consent based purely on information and consent based purely on trust might each be considered as extreme ends of a spectrum. Even when consent is based entirely on specific information processed by the participant, in some sense, this decision also depends on trust. After all, the participant must trust the source providing the information, or must trust that the information provided is truthful and complete. For the purposes of this paper, we will nevertheless consider these to be cases of consent based on information given the distinctive role that information processing has in the decision-making process. Similarly, consent based purely on trust may in various ways depend on information held by the consenter. A research subject's trust in a researcher may depend on general background information about that researcher, say, on her educational credentials, her institutional affiliation, or her moral character. Yet, considering that the consenter does not employ specific information about the nature of the proposed research in her decision-making process, we count such cases as instances of trust-based consent.

For the purpose of the discussion below, we will set these complications aside and focus on the paradigmatic cases of information-based consent and trust-based consent. We argue that under appropriate circumstances, consent based partly or even entirely on trust can be morally on par with consent based partly or entirely on information. That is, consent to participate in medical research on human subjects based on trust is not *per se* morally inferior to information-based consent.

4. The moral values underlying informed consent

We turn now to the moral values underlying informed consent. There is general agreement that the moral values central to informed consent include the values of autonomy; voluntariness; manipulation; and non-exploitation, and that these four values must be promoted and respected (Eyal 2012, Kleinig 2004, Nielsen 2010, Walker 2012, Faden & Beauchamp 1986). Informed consent is morally significant because it upholds these values in various ways. In what follows, we compare information-based consent with trust-based consent with the aim of demonstrating that the latter can promote and respect these values to the same extent that information-based consent can.

4.1. Autonomy

In this section, we offer an argument in support of the notion that consent based on trust can be no less conducive to the value of autonomy than consent based on information is.

Autonomy may be considered valuable for instrumental reasons or for non-instrumental reasons. Proponents of an instrumental defense of the value of autonomy in decision-making typically claim that autonomous decisions are generally more prudent (Mill 1859, Sumner 1996, Ladenson 1975). The corresponding claim is that informed decision-making generally leads to more prudent decisions than less informed decision-making does in comparable settings.

Other theorists hold that autonomy is valuable for non-instrumental reasons. Proponents of objective list theories of the good might hold this view (Parfit 1984, Griffin 1986). Here we may find the notion that exercise of autonomy is a fundamental good in individual lives. Thus, exercise of autonomy is valuable in itself. On the reasonable assumption that informed decision-making constitutes a form of exercise of autonomy, informed decision-making is intrinsically valuable independent of whatever instrumental benefits it might produce.

Now, our claim is that consent based on trust is not inferior to consent based on information with regard to its capacity to accommodate the underlying value of autonomy. This holds irrespective of whether the value of autonomy is defended instrumentally or non-instrumentally.

Consider first the view that autonomy is of instrumental value. According to this position, information-based consent promotes the underlying value of autonomy by simply being a form of exercise of autonomy, which is instrumentally valuable. We suggest that the same can be said about decisions based on trust, and moreover, that trust-based decisions may also be prudent.

It is, to be sure, a commonly held view that the thoroughly informed decision is the more prudent and thus the preferable one (Beauchamp 2011, Kleinig 2004). However, it seems evident that we routinely make decisions based not on specific information about the possible outcome of a certain course of action, but rather based on the trust we hold in the agent proposing said course of action. Suppose a good

friend of mine has taken me to dinner at his favorite restaurant, where I have not dined before. Upon being seated we are presented with an extensive and detailed menu, but before I start to consider my options, my friend suggests that he orders us both his preferred dish. Knowing that he usually has good taste and trusting that he would not order me something that I would not enjoy, I promptly close my menu and acquiesce. In this case, all relevant information about my options is readily available, but I ground the decision about my course of action in the trust that I hold in my friend regarding said course of action. Or, to take an example from the medical realm: suppose I go to see my family doctor, who has been treating me since I was a child (and my parents before me), with a nasty infection. My doctor has compassion with my suffering, and pulls out a powerful antibiotic from his medicine cabinet that he happens to have on hand, and recommends that I start taking it immediately to combat my infection. Feeling confident that he a) has the necessary expertise to know that the antibiotic will work against my infection, b) knows my medical history enough to safely assume that I will not have an unfortunate allergic reaction or the like, c) given our year-long personal relation has a genuine interest in my well-being, and d) that he, all the previous points aside, is under certain professional obligations and will be met with repercussions should he engage in malpractice; I feel grateful for his care and without asking further questions promptly start my antibiotic regimen.

These common decision-making scenarios show that we often base decisions about our actions – even ones that may affect our well-being – on our *trust* in the agents proposing them, and less on *information* about what they entail. This type of decision-making is not typically considered to be imprudent or irresponsible on behalf of the agent (under proper circumstances), and it would not be unreasonable for the agent to generally expect good consequences as a result of this type of decision-making. We believe that these observations are equally applicable to the decision to participate in medical research. Based on the assumption that two situations that share the same relevant features should receive the same normative evaluation, under proper circumstances, trust-based consent to medical research is no less prudent than consent based on information.[22]

So, if we hold that autonomy has instrumental value, we should interpret the value of information-based consent accordingly: information-based consent is valuable because it generally leads to prudent decisions. But trust-based consent under appropriate circumstances is valuable on the same grounds.

Now consider the view that autonomy has non-instrumental value. According to this position, information-based consent is valuable not (only) because of its instrumental benefits, but because it instantiates a form of autonomy; deciding based on information is to exercise one's autonomy, which is non-instrumentally valuable. Our claim is that a similar thing can be said about trust-based consent. Consenting on the basis of trust can itself be considered a way of exercising one's autonomy, and may thus be considered a species of autonomous decision-making.

In his influential account of autonomous action, Harry G. Frankfurt (1971) distinguishes between an individual's immediate desires on the one hand, and her more fundamental aspirations on the other. To do this, he introduces a distinction between first- and second-order desires. Here, a first-order desire expresses "what one wants" and has the form "agent A wants to perform action X", and a second-order desire expresses "what one wants to want" and has the form "A wants to want to perform action X". First-order desires are "effective" in that they are what drive the agent to action. Second-order desires are not effective in and of themselves, but inform the first-order desires that ultimately lead to the agent's action (Frankfurt 1971, pp. 7-10). According to Frankfurt, an agent acts autonomously either when her effective

[22] One may argue that the decision to participate in medical research is in fact qualitatively different from the type of standard, 'everyday' decisions considered here. We consider this objection below.

first-order desires match her second-order desires, or when the motivation for action flows from higher-order and not first-order desires. An important aspect of Frankfurt's account of autonomy is the assumption that an agent's true will is to be found in her second-order desires, in that these are the desires that she identifies herself with (ibid., p. 13). As such, the agent's second-order desires may be taken to be more deeply integrated in her self.

We argue that this view of autonomy is equally compatible with decisions based on trust on the one hand, and with decisions based on information on the other. In the context of decision-making regarding participation in medical research, this may be expressed in one of two ways:

> (1) An individual may have higher-order desires about the way in which she wishes to decide about her participation in a given study, namely that she wishes to base her decision on trust. This is often seen in cases where a potential research subject explicitly forgoes information about the study she is invited to participate in, with a justification along the lines of "they are medical professionals, I trust that they will not do anything that harms me or others" (Hall et al. 2001, McDonald et al. 2008, Kass et al. 1996). In such cases, the patient *decides* to consent based on trust rather than on information. As her decision follows the structure of autonomous decision-making, it is hard to see why this decision should be any less autonomous than had she decided to consent based on information (as it is the structure of the decision, not its basis, that determines whether it is autonomous or not).
>
> (2) When we trust, we are often aware of it and we can, at least to some extent, justify to ourselves and to others why we place trust in a particular person or institution – in other words, we are able to *actively reflect* upon our trust. This feature of trusting is comparable to Frankfurt's account of how we engage with our second-order desires. We may then say that we *identify* with our trust in a way that is comparable to how we (are able to) identify with our higher-order desires. If autonomy is exercised by acting in accordance with what one identifies with, there should be no relevant difference between deciding on the basis of trust and deciding on the basis of information. Decisions based on trust may thus be just as autonomous as decisions based on information. If so, trust-based consent does not realize autonomy to any lesser degree than consent based on information. Consent based on trust is thus a form of autonomy. If consent based on trust is a form of autonomy, and if autonomy is non-instrumentally valuable, then consent based on trust is also non-instrumentally valuable.

But what if you hold a different conception of autonomy than Frankfurt's narrow account? In much of bioethics, a broader concept of autonomy is dominant such that this notion is generally taken to refer to a capacity to shape one's life in accordance with one's preferences, values and life aims (see e.g. Beauchamp & Childress 2001, Dworkin 1988). On this broader conception, autonomy can be held to be instrumentally or non-instrumentally valuable, as discussed above. But in addition to what we noted there, it is worth observing two further ways in which autonomy (in this broader sense) may be morally important. First, individuals have the *moral authority* to make decisions for themselves and to make certain demands of others (including the demand that others do not do certain things without their permission). Second, individuals may have an *interest in being recognized as having the capacity for autonomy and being allowed to exercise it*. [23] On this broader conception, the paradigmatic exercise of autonomy with respect to information-based consent seems to conform to the following structure: firstly,

[23] We owe thanks to Tom Walker for this account.

the potential research participant is provided with relevant and appropriate information about the study, secondly she competently considers this information and thirdly she decides whether she will participate or not, based on her deliberation of the information that was informed by her own preferences and life aims.

It is our view that on this broader conception of autonomy, deciding on the basis of trust may be autonomous to the same degree as decisions based on information, and that trust-based consent may ultimately realize the same values of authority and recognition. To illustrate this, imagine a case in which a potential research participant insists that she does not need any information about the research that she is to participate in, and claims that she is fully comfortable leaving all details and technicalities to the researcher whom she trusts. If we take the moral significance of autonomy to be that the individual has the authority to make decisions on her own, then the research participant's decision to forgo information is still autonomous, as this decision is grounded in her own authority (just as it would be had she consented on the basis of the information that she was offered).

If, however, we take the moral significance of autonomy to be that individuals are recognized as having the capacity to make authoritative decisions, this could pose a challenge to the claim that trust-based decisions are no less autonomous than those based on information. After all, it seems counterintuitive to regard someone who uncritically allows important decisions to be made for her by others as having a healthy capacity for authoritative decision-making. To explain why this challenge is less troubling than it seems, consider again the restaurant case detailed above. In this case, it seems unlikely that anyone would regard my decision to let my friend decide what I will eat for dinner as evincing a lack of autonomy. This is because the particular circumstances are such that I have sound, informed reasons – namely, my prior experiences with his tastes, standards and his inclination to ensure that I get something I will enjoy – to confer the decision-making authority to him. In other words, an individual may have good, autonomy-supporting reasons for acting in a way that may *prima facie* seem to detract from her formal, personal autonomy.

These reflections also highlight that it is hardly ever the case that trust-based decisions are made without any information whatsoever. This information might just be of another sort than the specific information that is promoted by informed consent; instead it may be information that one has acquired through former experience with the trustee. In the restaurant case, available to me is information about my friend's usual tastes, standards and disposition to make sure that I get a meal that I will enjoy. And in the case of my family doctor, I have available to me information about his inclination to make sure I get the care I need and to minimize any suffering, in addition to my knowledge that doctors generally are under certain professional obligations and oversight, that standardly prevent them from engaging in harmful conduct towards patients. Similarly, the potential research participant has (or at least may have) at her disposal information about the perceived trustworthiness of the researcher and the research enterprise in general. If autonomy is exercised by considering available information and deciding on a course of action based on that information, and if information may be understood to constitute not merely facts about the possible consequences of a certain course of action, but more broadly to encompass background information such as past experiences with the agent proposing said course of action which elicit a sense of trust in the agent, then the types of decisions just accounted for should be deemed autonomous.

To sum up, in this section we have argued that consent to participation in medical research based on trust can be no less conducive to the value of autonomy than consent based on information is. This holds both whether autonomy is defended instrumentally or non-instrumentally, and whether understood in a narrow or broad sense.

4.2. Voluntariness, non-manipulation, non-exploitation

Besides promoting and protecting individual autonomy, informed consent is held to secure that individuals' decision to participate in medical research is voluntary, and is free from manipulation and exploitation. We take the values of *voluntariness, non-manipulation* and *non-exploitation* to be related issues in this context, and will thus discuss all three values in this section. Here, we demonstrate that in the context of decision-making, it is true for each value that *information* does not protect the consenter any more than *trust* does.

4.2.1. Voluntariness

Echoing a general credo of medical ethics, decisions to participate in medical research should be made on *voluntary* grounds (see e.g. U.S. HHS 1949, WMA 1964). So, voluntariness is a condition for the potential participant's consent to be valid. It is, however, not clear that *information* does anything to affect a decision's degree of voluntariness as compared to *trust.* In what follows we will argue that there is no case for claiming that a decision made on the grounds of information is *per se* any more voluntary than one made on the grounds of trust.

Voluntariness is commonly and broadly taken to mean the absence of coercion. The classical conception (see e.g. Aquinas 1273, Hobbes 1651, Locke 1823, Kant 1797) understands coercion according to the following formula:

> *Agent A coerces agent B when agent A enforces decisions about the activities of agent B by the use of force, violence or power.*

However, contemporary conceptions of coercion have taken a broader view, understanding certain threats or proposals as definitional of coercion. This modern line of thought has its roots in Robert Nozick's acclaimed paper 'Coercion' (1969), in which he identifies coercion with the implementation of *incentives* by agent A to make agent B take/refrain from taking action X. So, Nozick associates coercion not with the direct use of force or violence, but with conditional proposals, for example "If you do/do not do X, I will do Y/Z will happen" (where Y and Z are consequences agent B wishes to avoid). Since Nozick's analysis, many theorists have taken the issuing of a conditional proposal (in the form of either a threat or an offer) to be essential to the concept of coercion, though in need of some qualifications. Alan Wertheimer (1996) further qualifies Nozick's notion of the element of threat in coercion, claiming that the choice forced upon the coercee is such that she has *no reasonable choice* but to succumb to the proposed action. In other words, whether something counts as coercion is contextually dependent on the circumstances (more specifically, on the individual's *baseline* for normal course of events). As a supplement to this view, Joel Feinberg (1986) considers the central element of coercion to be active and successful intervention in the coercee's option set, ruling out the combination of noncompliance with the coercer's demand and the avoidance of unwelcome consequences. Fortunately, we do not need to settle on a precise theory of coercion here. We thus take voluntariness to mean the absence of coercion in the forms outlined above: coercion involves conditional proposals, and circumstances leaving an individual with no reasonable choice but to take a certain action if she wishes to avoid an unwelcome consequence.

If we understand coercion in this way, it is hard to see how information about outcomes should offer any safeguard against coercion that trust cannot offer to a comparable degree. The reason is the following: whether a decision's degree of voluntariness – or the degree or form of coercion involved in that decision-

making – is ethically problematic is determined neither by whether that decision is based on information nor whether it is based on trust. Rather, it is whether any of the elements associated with coercion accounted for above are at play in the decision-making process. Thus, the question of whether a decision is based on information or trust is orthogonal to the question of whether it is non-coerced. Consent based on trust can thereby be voluntary, and respect the value of voluntariness, in the same sense and to the same extent that decisions based on information can. Moreover, under similar circumstances, consent based on trust and consent based on information would typically be voluntary to the same degree.

4.2.2. Non-manipulation

Like coercion, manipulation is viewed as an immoral way of influencing individuals' decisions to participate in research. Hence, *non-manipulation* is another value that informed consent is held to protect: providing potential research subjects with all relevant and truthful information about a study is viewed as a way of ensuring that the decision they make is unmanipulated (as opposed to e.g. withholding information about side effects, or embellishing chances of therapeutic benefits).

Manipulation is different from coercion in that it does not directly interfere with a person's actions or option set, or change the cost of selecting a certain option. Rather, it is an *"[…] underhand interference with the ways in which people see their options"* (Wilkinson 2013, p. 345), and in this manner perverts the way a person makes decisions or forms preferences. However subtle an influence or interference, note that manipulation is always *intentional:* it requires an agent with an agenda that the manipulated acts or preferences ideally serve. As Martin Wilkinson (2013) points to, this *intention condition* is essential in explaining manipulation and its wrongness. So, whether a consent decision is manipulated – and thus ethically problematic – hinges upon whether it is underhandedly influenced by an agent with an intention to do so. If we understand manipulation in this way, it is hard to see why deciding on the basis of information *per se* offers a bulwark against manipulation: the information we decide upon may easily have been crafted and presented in a way that affects how we see our options (as is the case in much marketing). Whether it is or is not, is a question concerning the specific circumstances in which the decision takes place – not how the decision is reached. What about decisions based on trust, then? If we maintain the above account of manipulation in decision-making, it seems that trust, interestingly, offers a more robust safeguard against it: manipulation requires an active interfering agent with an intention; however, trust (cf. our account above) is usually an attitude that is developed over time, from numerous encounters with or impressions of the agent or institution in question. As such, we contend that trust does not lend itself to intentional perversion by singular agents as easily as other grounds for decision-making – for example information.

From these considerations we see that trust does not protect the value of non-manipulation to any lesser extent than information does – in fact, the opposite seems to be true.

4.2.3. Non-exploitation

As was the case with voluntariness, informed consent should be non-exploitative. Informed consent is valid only if it takes place in a non-exploitative context (Eyal 2012, Kleinig 2004, Nielsen 2010). A commonly accepted general formula for exploitation is the following:

A exploits B when A takes unfair advantage of B.

Excluding the large body of Marxist accounts (see e.g. Holmstrom 1997, Brewer 1987), the formula has been fleshed out in a number of ways that differ especially in respective interpretations of what constitutes the 'unfairness' criterion, i.e. what it means for an advantage to be unfair. While Allen Buchanan understands exploitation as *"the harmful, merely instrumental utilization of [a person] or his capacities"* (Buchanan 1985, p. 87), other writers maintain that it is (a) feature(s) of the exploitee's circumstances that qualify the interaction as unfair, and thus as exploitation. Joel Feinberg (1988) and John Lawrence Hill (1994) further highlight that exploitation involves the exploiter profiting by taking advantage of (a) specific feature(s) or vulnerabilities of the exploitee or her situation.[24]

The accounts above suggest that the unfairness criterion may be understood in one of two ways. First, it may be that the transaction between exploiter and exploitee is *procedurally unfair*, i.e. that there is a defect in the manner by which the exchange between exploiter and exploitee has played out (for example, if the exchange involves fraud or manipulation). Second, the unfairness criterion may be understood *substantively*, i.e. that the unfairness consists in it being wrong for the exploiter to profit at all from the exploiter (and her situation) (for example, if B has suffered a handicapping injury and A sells her a wheelchair at an excessively high price).

If we understand exploitation in either of the two senses outlined above, then whether a given setting is exploitative or not is a function either of the circumstances of the transaction or of the individual's option set (or potentially both). Hence whether a decision made within some setting is exploitative will depend on features of the situation in which that decision is made, and not on features of the decision-making procedure itself – in our case, whether it is based on information or trust. As such, these are equally irrelevant with respect to upholding the value of non-exploitation. Given this, it seems clear that decisions based on information and trust respectively realize non-exploitation to the same degree, in that they are equally immaterial to realizing it. Thus with respect to non-exploitation, consent based on trust is not morally inferior to consent based on information.

5. Conclusion

Throughout the analysis above, we have argued that consent based on trust has the potential to realize all four underlying moral concerns – autonomy, voluntariness, non-manipulation, non-exploitation – to (at least) the same degree that consent based on information does. On the assumption that when two practices accommodate the same underlying moral concerns to the same degree one cannot be morally inferior to the other, it follows that consent based on trust is not morally inferior to consent based on information.

6. Objections

In the following, we consider what we take to be the weightiest objections to our view that trust-based consent is not morally inferior to information-based consent.

(1) One possible charge might be that individuals consenting on trust may be more vulnerable to exploitation or other forms of abuse than individuals consenting on information, as in principle, a trust-based consent allows for withholding information from the consenter that might otherwise have influenced her decision to consent. This potential for "consent deceit" may, for example, be suspected in situations where patients are asked to participate in medical trials, and transfer their trust in their doctor as

[24] These two latter cases may also involve an issue of *defective consent*; see e.g. Zwolinski & Wertheimer 2015.

a caregiver to their trust in him or her as a researcher, thereby expressing a mentality of "you don't need to tell me anything about it, you're my doctor, I trust you" (Wadmann 2013, Kass et al. 1996). In such cases, it would seem fairly easy to withhold potential decision-affecting information from the individual, which would clearly constitute a violation of that individual. However, the liability here is to be found in the circumstances surrounding the consent; i.e. that the person seeking consent is not trustworthy – but not in the structure of trust-based consent itself. Furthermore, as we saw in our discussion of manipulation and exploitation above, providing information is not necessarily a safeguard against violation or abuse of (potential) research subjects. Here, individuals may just as well be violated should they be provided with false or misleading information, or should the choice set they are presented with be manipulated. Our claim is thus that in a setting absent of manipulation and exploitation, consent based on trust is not morally inferior to consent based on information.

(2) A related objection may be that information-based consent seems a more robust form of consent than trust-based consent, and that information-based consent is thus to be preferred on these grounds. Robustness concerns the ease with which a decision-making context can be turned into an imprudent, coercive or exploitative one, or one in which there are additional problems. The charge here is that even if consent based on trust is morally unobjectionable under appropriate circumstances, informed consent is nonetheless a more robust procedure.

We do not deny the intuitive appeal of this notion. That a strict set of formalities/procedures are typically involved in the practice of informed consent may give rise to the intuition that a process so thoroughly documented and rehearsed must produce comparably robust end results. Even so, we maintain that this intuition merely contributes to the *perceived* robustness of information-based consent as compared to trust-based consent. In practice, it does not do anything to tip the scale in favor of either model of consent. Robustness is not (only) a matter of providing information and securing documentation, but rather a function of circumstances relating to institutional accountability. In this respect, trust-based consent is no different than information-based consent: just as institutions (hospitals, public officials) can and should review procedures for informed consent, so can they review procedures for consent based on trust (and the options that potential trustees are invited to consider). We discuss institutional accountability in further detail below.

Note as well that one may encounter situations in which individuals from certain populations or cultures become suspicious as a consequence of being confronted with a large body of information that is difficult to comprehend. By lesson of this possibility, it may well be that in some contexts and cultures it is the very fact that a decision is based on trust that makes it robust compared to alternatives routes to decision-making. Several studies on informed consent in non-Western cultures support this suggestion (del Pozo & Fins 2008, Jafarey & Farooqui 2005, Packer 2011).

(3) The reader may have noticed that our claim that trust-based consent is not morally inferior to consent based on information hinges on the presupposition that decision-making takes place in appropriate circumstances, i.e. that the trust on which consent is based is not misplaced, and that the trustee is actually trustworthy. Given this, an obvious objection may be that it is easy to imagine instances in which the person seeking consent is not trustworthy, and/or in which the consenter is at fault for trusting someone she should not. Cases such as these would most likely cause instances of trust-based consent to fail on moral grounds. Note, however, that consent based on trust is no different than consent based on information in this respect: in the case of information-based consent, the consenter may misinterpret the information provided, or the information provided may be (deliberately) incorrect. Thus, our claim that trust-based consent is not morally inferior to information-based consent still stands.

(4) A final concern may be that there is in fact something special about decisions to participate in medical research, and that these kinds of decisions cannot and should not – as we claim above – be compared to other garden-variety decisions and the demands associated with them. This line of objection might maintain that a decision to participate in medical research may be very different from the decision to accept a meal suggestion at a restaurant on a number of different parameters: a) in many cases there is much more at stake (for example, health risks and possible reductions in well-being), b) participation in research does not (necessarily) benefit the individual directly, and c) the individual's participation may have consequences on others (for example, on family members or, with some types of research, on future generations). These considerations, it might seem, ought to raise the standard for a more rigorous and thorough decision-making scheme, and to some, it may seem that information-based consent is more apt than trust-based consent to provide this.

However, this intuition may very well rest on the same factors that we accounted for with regard to the notion of robustness above, and we thus reiterate that these factors do not necessarily have any real effect on the actual quality of the resulting decision. While we agree that there may be something to be said for the difference in decision-making in terms of the potential moral weight of a decision's consequences, with research participation on the one hand and dinner options on the other, it is clear neither that nor why *information* should be thought to provide a solid foundation for proper navigation here. All that the objection demands is that decisions regarding research participation are undertaken in a manner more rigorous, and should be subject to more careful consideration, than most of our everyday decisions. Accordingly, we venture that there may be other, non-informational routes to achieving this goal, and deciding on trust is a valid candidate.

7. Concluding remarks

7.1. Pragmatic arguments for IC

We have argued that trust-based consent is not morally inferior to information-based consent in that both decision-making procedures observe and respect the relevant underlying moral values to at least the same degree. However, some may insist that there are nonetheless strong *pragmatic* reasons for preferring consent based on information when subjects are invited to participate in research: providing comprehensive information as part of the consent process may educate potential consenters, and employing and promoting a practice of written communication may function as an incentive for certain groups of potential consenters to learn to read and write (Nyika 2005, Benatar 2002, Sherman et al. 2012, Ezeome & Marshall 2009). In other words, employing informed consent may produce positive externalities.

We acknowledge that in specific situations and circumstances the potential for positive externalities may count in favor of adopting a scheme of informed consent rather than trust-based consent, but this is peripheral to our conclusion that trust-based consent is not *per se* morally inferior to informed consent. On the contrary, we maintain that our conclusion is in fact fully compatible with the pragmatic considerations accounted for here.

7.2. How to safeguard against misplaced trust?

Trust relations – be they in medical practice or other human affairs – can go wrong. We may place our trust in someone who we should not have, someone who turns out to be *untrustworthy*. The history of

medical practice and research offers several grim examples of this.[25] This has led many to hold that trust is too thin to function as an ethical safeguard in matters of consent, often concluding that reliance solely on trust is unacceptable. Neil Manson and Onora O'Neill assert that a suspicion of trust is central to much contemporary autonomy-based bioethics, reflecting fears of misplaced trust and the high costs associated with it, and they note that in the context of this debate it is commonly claimed that trust is *"…intrinsically immature, risky and unintelligent"* (Manson & O'Neill 2007, p. 159). We agree with Manson and O'Neill that this prevalent stance overlooks the fact that all trust may not be blind, and that it is in fact possible to trust intelligently. Manson and O'Neill suggest that trustworthiness in research practice may successfully be supported and furthered in research practice by *systems of accountability,* that "define, assign and help enforce second-order obligations to account for the performance (or non-performance) of primary or first-order tasks or obligations" (see p. 167-182 for their full account of the formal structure of accountability). A robust system of accountability provides adequate guidance for individuals to place trust intelligently, thus improving trustworthiness, and to some extent eliminating the risk of misplacing trust. This is not least relevant in the context of medical research, where – as we have seen – information often takes a backseat to trust in many actual instances of consent.

7.3. Implications for practices for ethical committees

Above we made the observation that consent to medical research is often neither based entirely on information nor trust, but a blend of these two – commonly with trust playing the lead role. With this in mind, it appears that ethical committees tend to place a disproportionate weight on the information component in consent (focusing on the detail, level, of the information in informed consent forms; the manner in which it is disseminated, etc.), often overlooking the importance of the trust-relations in which the information is communicated. This may devaluate the efforts researchers do make with the aim of being trustworthy (for example through accountability and transparency regarding governance mechanisms, but also through the specific strategies informed by local customs researchers employ when recruiting research subjects in indigenous cultures).

7.4. Implications for broad consent to genomics and biobank research

Much debate surrounds the ethical tenability of giving broad consent to genomics and biobank research (see e.g. Hanson 2006, Sheehan 2011). This divided debate is contrasted by the dominantly positive attitude of the public with respect to giving broad consent to this type of research. Refraining from going too far into this discussion, we would like to note that giving broad consent strikes us as a quintessential example of consent based more on trust that information: specific information about the research does not play a role because it is simply not available; and thus the research subject's consent is based on the *trust* she holds in the researcher or research enterprise, and how they will (not) utilize her sample and/or data. If our conclusion that consent based on trust is not morally inferior to consent based on information is correct, this provides yet another reason that broad consent is not as morally suspect as some authors hold – especially if mechanisms of accountability, as discussed above, are in place.

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[25] One is the Tuskegee syphilis study, see e.g. White 2000.

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Article 3: Exploitation and vulnerabilities in biobanking in developing countries

1. Introduction

Much important work has been done on the subject of exploitation of individuals in developing countries in clinical/medical research (Resnik 2003, Macklin 2003, Hawkins & Emanuel 2008, Gbadegesin & Wendler 2006). Here, authors have typically assessed randomized controlled trials and placebo studies. However, not much work has been done on the subject of exploitation in the context of research biobanking. This type of research differs in important respects from the aforementioned (and other relevant) types of medical research: typically, the risks and harms associated with donating a sample for research is negligible compared to e.g. drug trials and other invasive procedures, and the benefits for both researchers and research participants stemming from the biobanking directly are not as easily captured as in trials of certain drugs or procedures. This means that the accounts offered regarding exploitation in medical research involving individuals in developing countries may not be fully, or easily, applicable to the context of research biobanking: some features that may be grounds for exploitation in clinical research is not relevant in the context of biobanks; conversely, the context of research biobanks may offer grounds for potential exploitation that do not arise in clinical research. To get a clear picture of what exploitation may look like in the specific context of biobanking in developing countries, there is a need to start over and re-apply the common exploitation framework to this particular context.

This is the aim of this paper. In Article 1 I, along with my co-authors, reported on an interview study with Pakistani biobank donors conducted in April 2014. While conducting these interviews, several features of the setup and relation between researchers and donors struck us as possible ground for exploitation. As a way of thoroughly investigating and articulating this uneasy intuition, the following will be an analysis of this case from the point of view of the standard theories of exploitation. I have grouped these into Kantian, unfairness-centered and circumstance-centered theories, respectively, and I will argue that the latter group fares best with respect to capturing and explaining our intuitions about the case vis-à-vis exploitation. Ultimately, however, I will argue that the standard exploitation theories overlook relevant features of the case (and thus only give us half the picture), and employing a more refined view of what constitute vulnerabilities can elucidate some otherwise hidden features of our case that may be grounds for exploitation.

At the outset it should be noted that the vast body of philosophical literature on the concept of exploitation presents a rather murky territory, with a plethora of more or less diffuse interpretations of this concept. At best, we can say that there is no general philosophical agreement as to just what exactly constitutes exploitation. Instead of wading too deep into these conceptual badlands, my strategy will be to take the point of view of some of the dominant theories of exploitation to investigate how they apply to our case. As such, this paper is an explorative one; in that it identifies a selection of notions of exploitation and vulnerability, and investigate whether and how these are expressed in the Pakistan case.

To begin, however, I will first briefly sketch some relevant features of research biobanking, and subsequently account for our case of research biobanking in rural Pakistan, which will be the subject for my analysis.

2. Biobanks

Biobanks are biorepositories that store human biological samples for use in research. Samples (most commonly of blood, skin or other tissue) are linked to genetic information about their donor. Sample donors may be individuals from a population with (a) certain disorder(s), providing material for research into that/the specific disorder(s)[26], or samples from healthy individuals for control.[27] Samples can be constituted of leftover human tissue from surgery (e.g. tumors), or human material that is actively donated from participants from a certain population of interest (usually by giving a blood sample).

Biobank samples are typically used in genome-wide association studies, using large collections of samples to identify biomarkers for disease; in the development of personalized medicine; or to uncover the genetic basis for certain genetic disorders. As biobanks function merely as the storage and provider of material for a variety of research, there is no direct research outcome – and thus no direct benefits – from biobanks as such.

3. Case: collection of samples for research biobanking in rural Pakistan

The subject of analysis will be the case of collection of blood samples from individuals from rural Pakistan, detailed in Article 1. Let us recall the contours of this case:

> Researchers from an institute for genetic research located in Faisalabad are conducting research on an array of genetic disorders. These autosomal recessive genetic disorders of various kinds are highly prevalent in the villages and rural areas surrounding Faisalabad, due to the local practices of consanguineous marriages, and are, in virtue of the genetic heritability, incurable as such, and typically no treatment is available.
>
> To collect samples, researchers travel to donors' locality and encourage them to donate blood samples informing the donors that their samples will be used in research on their disorder (and perhaps related disorders), which may down the line lead to insights into how to control and prevent the particular disorder that affects the donor's family.
>
> The donors are poor, largely illiterate and uneducated, and generally find it difficult and stressful to cope with their disorder under circumstances of few individual resources and poor medical infrastructure. They are part of a hierarchic, patriarchal and religion-centered societal structure, placing authority, honor and responsibility on family elders, educated people, and medical professionals. Donors are generally unfamiliar with the difference in nature between medical therapy on the one hand and therapy on the other, and associate the practice of taking blood samples with what a doctor does in order to ascertain and initiate proper treatment. Thus, they come to believe that the researchers are medical doctors, and that their donation of blood samples will result in a treatment or cure for their family disorder.

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[26] Fx the *Infectious Diseases Biobank* at King's College London, UK (http://www.kcl.ac.uk/lsm/research/divisions/diiid/about/facilities/biobank/index.aspx [accessed March 29 2016]), or the Mitochondrial Disease Biobank at the Mayo Clinic, USA (http://www.mayo.edu/research/centers-programs/mitochondrial-disease-biobank/overview [accessed March 29 2016])

[27] Fx *PKU-registret* at Karolinska Universitetssjukhuset, Sweden (http://www.karolinska.se/for-vardgivare/kliniker-och-enheter-a-o/kliniker-och-enheter-a-o/karolinska-universitetslaboratoriet/cmms---centrum-for-medfodda-metabola-sjukdomar/pku-biobanken/; [accessed March 29 2016]); or *The Danish Neonatal Screening Biobank,* Denmark (http://www.ssi.dk/Diagnostik/Center%20for%20Neonatal%20Screening/Den%20Neonatale%20Screenings%20Biobank.aspx, [accessed March 29 2016])

When approached by the researchers, donors are thrilled and relieved to receive medical attention to the disorder in their family by highly educated medical professionals, and happily agree to give blood samples to the researchers.

Consulting the literature on medical research in developing countries, it becomes evident that this is a common way of conducting genetic research in developing countries with populations such as the one mentioned above, and the donors' reactions echo those of other research subjects in similar contexts (Wonkam 2011, Kamuya et al. 2014, Nyika 2009, Gikonyo et al. 2008, Tindana et al. 2012). I thus take this case to be representative for a larger field.

4. Theories of exploitation and application to the Pakistan case

As already indicated, exploitation is a contested topic in the philosophical literature. In the following I will not engage in an in-depth analysis of this concept, but rather present different families of theories of exploitation to see what they each have to say about exploitation in the Pakistan case.

After conducting a survey of the (vast) literature on the topic of exploitation, I have grouped the dominant theories into three 'families', according to what they take to be the defining (or wrong-making) feature of exploitation. Note that this grouping is merely to be viewed as a tool for the following analysis, and that some of the theorists mentioned may disagree with my placement of them. Be that as it may, I maintain that my grouping is warranted with respect to my particular errand. These families are as follows:

i. Kantian theories
ii. Unfairness-centered theories
iii. Circumstance-centered theories

In the following, I will analyze the Pakistan case from the point of view of each of these families of theories, with the aim of answering the question of whether our case is one of exploitation on the respective accounts.

4.1. Kantian theories

One family of theories of exploitation take as their starting point the philosophy of Immanuel Kant, more specifically his famed *categorical imperative* (CI). In Kant's writings, this is spelled out in two formulations:

1) The Formula of Universal Law: *"Act only according to that maxim by which you can at the same time will that it should become a universal law"* (Kant 1993, p. 421)
2) The Formula of Humanity: *"Act in such a way that you treat humanity, whether in your own person or in the person of another, always at the same time as an end and never simply as a means"* (ibid., p. 429).

Several Kantian exploitation theorists further connect the second formulation to another of Kant's principles, namely the irreplaceability of persons, articulated in the distinction between *price and dignity: "Whatever has a price can be replaced by something else as its equivalent; on the other hand, whatever is above all price, and therefore admits of no equivalent, has a dignity"* (Kant 1785, p. 53). According to this principle, persons have dignity and cannot be replaced. Treating persons as interchangeable is to regard them as having mere 'price', and fails to respect their inherent dignity.

Exploitation theories resting on this theoretical background take the defining feature (and in some but not all cases, the moral wrong) of exploitation to be that exploitative interactions treat (potential) exploitees either as merely means to a certain end not of their own, or that they regard them as interchangeable units, or both. We may thus put forth the following formula for this interpretation of exploitation:

> *A exploits B iff A brings it about that B, or some part or aspect or behavior of B makes a causal or constitutive contribution to the achievement of A's relevant goals, that B does not share.*

As an example, Stephen Wilkinson understands exploitation along these lines, in the sense of *instrumentalization*:

> *"[e]xploiters [...] necessarily use others to foster the achievement of their own goals: goals which may or may not be selfish, and may or may not coincide with the furtherance of their real interests."* (Wilkinson 2003, p. 21)

This is what Wilkinson terms "the use condition", and this is not necessarily to be understood in a moralized sense – that is, claims about exploitation are not in themselves claims about the occurrence of a moral wrong:

> *"[f]or A to use B is simply to bring it about that B, or, more likely, some part or aspect or behaviour of B, makes a causal or constitutive contribution to the achievement of A's relevant goals"* (ibid., p. 22).

Now, it does indeed seem that we very often use other persons like this (such as when I, after a long grueling week of writing, go see my massage therapist for her skills in bringing my shoulder back to their proper place). However, according to Wilkinson, what makes exploitative interactions morally wrong is that they include a *wrongful use*. A use of a person is wrongful when it violates the second formulation of Kant's categorical imperative, i.e. when we use someone *merely* as a means to an end – that is, use them in a way that does not acknowledge that they are ends-in-themselves who have interests of their own (e.g., should I fail to acknowledge that my massage therapist has life goals worth of respect, and thus refuse to pay her a proper amount for her services that would allow her to pay her rent and feed her family). In arguing for this, Wilkinson further turns our attention to Kant's thought that when we become focused on a person's value with respect to their usefulness to us, we have a tendency to disregard the fact that she is an end, too (ibid., p. 37).

A similar, but slightly different account is offered by Ruth Sample (2003), in which she unfolds her notion of exploitation as *degradation*. Sample agrees that the defining structural feature of exploitation is that it is fundamentally using someone as a means to an end (Sample 2003, p. 15). However, Sample contends that what makes exploitation wrong is not just that we treat a person merely as a means to an end, but that exploitative interactions are morally wrong because they fail to respect the inherent value in that person, hereby *degrading* the person. Degrading is to be understood as reducing our view on someone from something unique, with dignity and interests warranting respect; to something replaceable with a price, a mere thing or object:

> *"Exploitative interaction, then, can be seen as a particular kind of disrespect toward a person in pursuit of our own advantage – the disrespect of merely using another person. "Merely using" is to be understood as refusing to acknowledge the value of our interactor by refusing to take her genuine interests seriously"* (Ibid., p. 70).

Both accounts are supported by Kant's caution against using others as means to an end, but they differ in that Wilkinson's account relies mostly on the second formulation of the CI (the moral obligation to never

use persons as mere means-to-ends), whereas Sample's relies more on Kant's notions of dignity and fungibility,[28] and the disregarding of persons' value.

An alternative Kantian account of exploitation related specifically to the field of medical research in developing countries is put forth by Andrew W. Siegel (2006). From the first formulation of the CI, Siegel derives a *duty to beneficence,* understood as the moral obligation to do what we can to help persons preserve their status as agents (Siegel 2006, p. 181), i.e. fulfilling the "true needs" of persons: those that are crucial to maintaining their status as rational agents (this may be translated to minimal living requirements, medical aid etc.; ibid., p. 188-189). On this account, to exploit others is to use them for the advancement of a certain goal, in a way that is displays indifference to the conditions for preservation of their status as agents (e.g., by failing to provide relevant benefits and/or compensation). Siegel takes this indifference to be a violation of the obligation to respect persons' value as rational beings.

Now, the practice of using persons as means to an end applies to all medical research involving human subjects, in the sense that the subjects are necessary 'tools' to carry out the research.[29] Researchers enroll subjects in clinical trials and other medical research not for the sake of this practice on its own, but to further another goal: the advancement of the understanding of certain disorders and of effects of certain drugs, and the development and improvement of treatment regimes and technologies. This is arguably all directed towards the (very) general goal of better health and livelihood of humanity, or the more narrow goal of benefiting a particular kind of patients – as such an overall noble pursuit and one that carries moral weight. At the same time, however, we should recognize that researchers also engage in the recruitment of research subjects as a means to the end of their specific research projects, and thus as a means to further their own academic career. This is not something that we usually object to – rather, it seems to be a condition interwoven in the nature of much academic research involving human subjects and its aforementioned goals. Furthermore, as Wilkinson points out, we are not necessarily to understand the fact that someone uses someone else to further his goals in a moralized sense, i.e. that it is necessarily a moral wrong to use someone else to reach a certain goal – as pointed out above, this is something we very often do. It is not morally wrong for a researcher to use subjects as a means to reach the end of her research project or, for that matter, in this pursuit at the same time also attend to considerations regarding her own career advancement. For a researcher to use her subjects in a morally wrongful way – to exploit them – is to use them *merely* as tools or material to pursue whatever end the research project sets out, and in this way to regard them as interchangeable and fungible units without dignity and own aims (by not properly recognizing and protecting their interests); and, to use Sample's terminology, to *degrade* them.

4.1.1 Application to the Pakistan case

Let us now apply these considerations to our case. To determine whether it involves exploitation in the Kantian sense, we must look at whether the donors are being regarded or treated as *mere means.* As discussed above, to regard a person as more than mere means (i.e. as an end in herself) is to recognize and respect her own relevant interests and inherent and non-negotiable value as a rational and autonomous being.

Firstly, the researchers' primary aim is clear: they wish to utilize the subjects, or more precisely, just a part of them (their blood sample and the information that may be derived from it) to further their own

[28] I.e., a good or asset's property of interchangeability with other individual goods or assets of the same type.
[29] Note that this claim does not rule out that some research subjects may rightfully and reasonably participate in research to further their own interests; e.g. clinical trials where some patients get a promising treatment. In any case, the point I wish to stress is that even in such cases, the research being carried out necessarily uses these same patients as means to further its goal.

goal, set out by the research they are conducting on rare diseases. As such, their interest in the subjects is largely instrumental and guided by the (potentially high) utility of the samples. Secondly, it can be argued that in a sense, due the nature of the research, once their samples are taken the donors relinquish their inherent uniqueness and personal goals: in the light of the end set out by the research, donors' individual contribution and participation could, in principle, easily be replaced by one from any other donor that met the same relevant functional criteria (i.e., suffered from the same disorder).

It seems that the concern articulated by Wilkinson, that we tend to forget persons' interests and inherent autonomy when we become aware of their usefulness to us, informs many claims about exploitation in medical research. As an example, George Annas and Michael Grodin state that

"[u]nless the interventions being tested will actually be made available to the impoverished populations that are being used as research subjects, developed countries are simply exploiting them in order to quickly use the knowledge gained from the clinical trials for the developed countries' own benefit" (Annas & Grodin 1998, p. 561).[30]

From the conditions laid out above this concern can certainly be raised with respect to our case as well: we can imagine that the researchers may be 'blinded' by the value of a particular family's samples, having the potential to result in a breakthrough in their work and career, and become fixated doing whatever it takes to secure samples from the family; without due considerations of their preferences, goals and feelings.

On closer inspection, however, it seems as a very strong claim that when we become aware of someone's usefulness to us we automatically come to regard him or her solely as a means to our own end, entirely disregarding his or her value and autonomy. I find my close friends' ability to make me laugh and their support in tough times very useful with respect to my own interests, but that does not rule out that I at the same time can recognize their value, autonomy and dignity. Furthermore my enjoyment of their talents could not meaningfully be described as exploitative (at least not in the absence of additional qualifications).

If the claim that recognizing someone's usefulness to us necessarily means that we disregard them being an end in themselves is implausible, then charges about exploitation rooted in this claim – such as that when researchers come across 'useful' research subjects, they come to view them merely as means, and that this amounts to exploitation – are too. Then, just because the researchers view the subjects as useful, this does not necessarily mean that they treat them as mere means, and thereby exploit them.

The next question to ask is then whether the donors are being treated more than mere means. To do this, their autonomy, value, dignity and interests must be properly respected, or, at least, not be ignored or overruled. Is this the case? To answer, let us look at (what we can reasonably assume to be at least some of) the interests of the donors. In a sense, we can say that they share the goal of the researchers, i.e., to develop understanding of and treatment against the disorder in question.[31] A different way of stating this is that the respective interests of the researchers and donors in developing in the understanding of the relevant disorder overlap, albeit stemming from two different sorts of motivations (academic motivation for the researchers; personal motivation for the donors). An alternative interpretation of the situation is to say that the goals of the researchers and the donors are in fact different: the researchers wish to further their scientific work; the donors wish to acquire some form of help for their family disorder. However this

[30] Similar claims are offered by Bayer (1998) and Crouch & Arras (1998).
[31] It can be argued that having a shared goal does not necessarily exclude that one may be used as means by the one with whom ones shares this goal.

does not necessarily mean that the donors are being used as mere means in their inclusion in the research; namely if they in virtue of their participation pursue their own goal. In this case, we can say that the researchers and the donors pursue the same path to each their goal.

If the research the donors were enrolled in did nothing to serve their own interests (setting aside questions of consent to such an arrangement), then they would likely be treated as mere means to an end. But as I have just unfolded, we have no reason to think that this is the case. In conclusion, given that there is no reason to suspect that the research subjects are treated as *mere* means in our case, this is not a case of exploitation on the Kantian interpretation.

Here, it is possible to object that we still exploit when we do not "give back" to an appropriate extent – that is, in order to appropriately acknowledge someone else as an end in themselves, we must, when we use them as means, offer compensation that adequately acknowledges them as ends in themselves. This is a valid (and much discussed) concern in the context of multinational research, but it seems that it is not properly explained by reference to Kantian terms. What this intuition points to is the notion of *unfairness* as a central element in exploitation, which I shall turn to now.

4.2. Unfairness-centered theories

Another family of exploitation theories takes the fundamental wrong of exploitative transactions to be that they are *unfair*, typically in the distribution of benefits between the exploiter and the exploitee, or how this has come about. I shall focus mainly on Alan Wertheimer's account, but Joel Feinberg and Robert Mayer advance similar theories (with some internal disagreement, on which I will comment where relevant).[32] According to these theories, exploitation has to do with the distribution of benefits between the parties of a transaction – most commonly one where one party of a transaction benefits far more than the other, and this distribution is an expression of unfairness. As a general formula for this type of theories, we may use Wertheimer's:

> *"[a]t the most general level, A exploits B when A takes unfair advantage of B"* (Wertheimer 1996, p. 10).

On Wertheimer's account, this unfairness may come out in one of two ways. Firstly, it may refer to some dimension of the *outcome* of the transaction or exchange we hold to be exploitative. This commonly refers to that the benefit for the exploiter is excessive compared to the benefit for the exploited, or that the exploited takes on risks or harms that are unfair seen in the light of the benefit he receives. A paradigm example is that of sweatshop labor: the employer benefits far more from the workers labor than they do themselves, and depending on the nature and duration of work, the laborers may be subject to harms and risks that are nowhere near adequately compensated for via their minimal wage. In this way we may say that the exploitative act has an unfair *benefit profile.*[33]

However, this is compatible with what Wertheimer calls *mutually advantageous exploitation.* In contrast to harmful exploitation, which leaves the exploited party worse off following the transaction, mutually advantageous exploitation is a case where the exploited party benefits as well as the exploiter, compared

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[32] Alan Wertheimer holds that exploitation is a case of *excessive gain*, i.e. that one party of a transaction benefits far more than he should compared to the other. Robert Mayer claims that exploitation is an instance of *wrongful gain;* more specifically a failure to benefit others as fairness requires.

[33] Or, as other theorists suggest, when B benefits, but the transaction inflicts unfair substantive harms or costs upon B (resulting in an unfair net effect on the benefit profile). Whether harm to B is a necessary condition for exploitation is a point of disagreement. See Zwolinski & Wertheimer 2015; Mayer 2007, p. 144-145.

to a non-transaction baseline. She is, however, still harmed according to what fairness requires, i.e. how much she *ought* to benefit from the transaction (balanced with potential losses, in one sense or another). As an example of mutually advantageous exploitation we may again turn to that of sweatshop labor: the workers do benefit compared to not being employed, but are still harmed according to how much they *ought* to gain. Even though they benefit, the benefit profile is unfair. This raises the point that we cannot evaluate the fairness of a transaction solely by comparing the benefits of the parties (from a non-transaction baseline), but must also measure the benefits of the respective parties against a normative baseline of what they *ought* to gain (or pay). However, this fairness baseline may not be easy to specify. In some cases, it can be helpful to refer to a (hypothetical) market price for a good or service, as shown in Wertheimer's famous snow shovel example:

> *"An unexpected blizzard hits an area and people rush to the hardware store to buy a shovel. The hardware store owner sees the opportunity to make an abnormal profit and raises the price of a shovel from $15 to $30. […] Both parties gain. But B feels exploited because B gains less (or pays more) than B thinks is reasonable."* (Wertheimer 1996, p. 22.)

Here, the reason that the transaction is unfair is that there is a relatively fixed market price (which we hold to be reasonable) for snow shovels, and charging B double that amount for the same good is in effect held to be unreasonable. However, the fairness baseline does not necessarily have to do with the market price of a good, and from a fairness baseline point of view an exploitative transaction may, paradoxically, benefit the exploitee more than the exploiter (but still be unfair). Take for example Wertheimer's unfair surgery example (Wertheimer 2011, p. 208):

> Surgeon A knows that all other surgeons in the area are on vacation. Patient B will die without surgery. A proposes to perform the life-saving surgery on B for three times his normal fee. B accepts. A gains a lot, but not compared to B (who "gains" his life).

Here, the fairness baseline is not only concerned with a market price (as it is, for most intents and purposes, meaningless and impossible to put a price on a human life), but also that it is the normative obligation of the surgeon, qua his profession, to save the life of the patient and not seek to, first and foremost, make a profit on this. These considerations indicate that where the fairness baseline is drawn, and what defines it, varies highly from one case to another and depends on the specific features of that case. In some cases we have fairly established intuitions of where the fairness baseline should be drawn – but in some we do not. This point becomes no less relevant in our biobanking case (and also in the general context of certain emerging other (bio)technologies): we do not yet have as established intuitions or ideas about the value of a blood sample, or the moral obligations that derive (or do not derive) from this value, as we do with respect to human lives or snow shovels.

Secondly, 'unfairness' may refer some defect in the *process* by which the unfair outcome has come about. This can concern the formation of the agreement between A and B such that the circumstances for the exploitee's informed and voluntary choice to engage in the transaction has been compromised; e.g. by coercion, fraud or misinformation. In contrast with other accounts, Wertheimer understands coercion as *"rendering B's consent unfree or involuntary by altering the objective circumstances under which B chooses"* [34] (Wertheimer 1996, p. 256), rather than actively and intentionally altering B's capacity to

[34] To illustrate, take an example from the movie *Godfather;* when Don Corleone makes the film producer who has turned down Johnny Fontane "an offer he can't refuse": there is nothing suspect or unreasonable about the contract

make decisions or to "reason effectively" (Hill 1994, p. 637). A coerces B to do X when he threatens to make B worse off with reference to some baseline, if B does not do X. Fraud and misinformation work in the same structural way, leading B to make a decision she would not make, had the information available to her been different (and where A benefits from this decision). Fraud and misinformation (for example, when A is attempting to sell his used car to B, and sets back the odometer from 50.000 to 10.000 miles) undermine the validity of B's consent to the transaction, because valid consent presupposes that it is made on the basis of facts that are in line with reality (Wertheimer 1996, p. 26). We should note here that it seems plausible to expand our conception of misinformation in the following way: misinformation may not only refer to giving false information, but may also be providing inadequate information (for example, deliberately withholding information that one knows is relevant for the other party), or presenting information in a way that one knows will elicit a certain reaction or belief with the other party (for example, exaggerate the party's belief regarding the likelihood that some event that has significance to the other party will happen, following her choice of action).

With respect to both coercion and fraud/misinformation, A uses *illegitimate* strategies so that B chooses an action that he would not have in a setting without A's interference, with A's aim of benefiting from this particular action on the part of B. This constitutes unfairness in the process of a transaction. This is morally problematic primarily because it is A who creates the distortion in B's objective circumstances as a means to his own benefit.[35] Note that this type of situations – where A coerces or misinforms B – are very different form situations where B is compelled by his circumstances to make a certain choice, that happens to benefit A. There is disagreement over the extent to which highly unfortunate and pressuring circumstances make consent invalid, and in effect undermine the choices that are made under such circumstances. I will engage in this discussion in the following section, but for now it is sufficient to note that I agree with Wertheimer and others that inequality of bargaining power or unfavorable circumstances, or the fact that a choice is made under unfortunate circumstances, does not make the choice invalid with respect to consent.

We have now established that according to Wertheimer and related theorists, unfairness as the defining feature of exploitation may concern either the distribution of benefits, or the way in which the distribution has come about. It is worthwhile to note that much work on exploitation in medical research in developing countries tends to employ an unfairness-based understanding that emphasizes the distribution of benefits between the researchers (often from a developed country) and the research subjects in the developing country. Therefore I will briefly give an overview of this dominant account, before zooming in on how it applies to our biobank case.

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being drawn between the producer and Fontane itself, but as a means to manipulate the film producers circumstances for choice of action, Corleone includes elements that are normally not part of the practice of drawing contracts (namely the severed horse head that constitutes a threat), and thus breaches the rules of the game.

[35] Alternatively, it may also be the case that A takes advantage of some feature of B or her situation, e.g. a disposition or character trait, that is simply there – e.g., as exemplified by Joel Feinberg (1988), A may take advantage of that B is caring or trusting or loyal (Feinberg 1988, p. 179). This is, however, not controversial: e.g. on hot summer days, park ice cream vendors take advantage of pedestrians' pre-existing desire to be cooled off; without this being a cause for moral complaint. What turns such transactions from trivial to unfair is when the exploiting party deliberately and, most often, sneakily "[*play*] *on some character trait of the other for the purpose of securing some advantage"* (John Kleinig, in Feinberg 1988, p. 178). This is, however, a different strategy for explaining the moral wrong in exploitation, which I shall discuss in the following sections discussing vulnerabilities.

4.2.1 Unfairness in accounts of exploitation in medical research in developing countries

Unfairness in medical research in developing countries is generally taken to concern the allocation of *harms/risks and benefits* in the relationship between researchers and research participants – more precisely, the *harms/risks* and *potential benefits* to the research participants, and the *benefit*s to the researchers (see e.g. Ganguli-Mitra 2012 & 2013, Resnik 2003, Macklin 2003). This may be understood in two senses. Firstly, it may be understood as that the *harm/benefit profile* of the individual's participation in a given study or trial is eschewed in an unfair manner, i.e. that the harms (or risks of harm) the individual takes on are excessive as compared to the (potential) benefits he or she receives from it. An example of this line of reasoning is found in Gbadegesin & Wendler (albeit with respect to communities):

> *"The fairness of the benefits that a community receives as part of its involvement in a research study depends upon the risks and burdens that the community bears as a result of its involvement in the study. In general, the greater the risks and burdens a community bears, the greater benefits it should receive".*[36]

In the developing world context, this may be observed in cases where individuals due to their circumstances and desperation for medical attention and/or hopes of any alleviation or treatment accept grave risks or side effects associated with the trial, with little actual benefit.

Secondly, it may be understood as an *unfair distribution of benefits* between research subjects on one hand, and researchers/sponsors/individuals other than the research subjects on the other. As Ruth Macklin illustrates, a common setting for this type of unfairness is multinational research in which the investigators or sponsors and from a powerful industrialized country, and the research is conducted in a developing 'host country' (Macklin 2003) – with the added complication that the population in the developing country often will not be able to afford the resulting treatment or product, and thus do not benefit fairly from their participation. This is usually referred to "the problem of reasonable availability" (Hawkins & Emanuel 2008, p. 9), and articulated by e.g. Annas & Grodin (1998):

> *"Unless the interventions being tested will actually be made available to the impoverished populations that are being used as research subjects, developed countries are simply exploiting them in order to quickly use the knowledge gained from the clinical trials for the developed countries' own benefit*" (Annas & Grodin 1998, p. 561).[37]

These two ways in which research can be exploitative echo Wertheimer's first sense of unfairness; outcome unfairness: the research is exploitative because it does not benefit the research subjects as fairness requires. The research subjects do not gain as much as they ought to, where what they ought to gain is specified in relation to the risks/burdens they take on and/or how much the researchers benefit.

4.2.2. Application to the Pakistan case

Let us now see how these considerations apply to our case, starting with unfairness as concerned with the harm/benefit profile of the research. In contrast to clinical trials, where a drug might induce unforeseen

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[36] Gbadegesin & Wendler 2006, p. 251.

[37] There are several well-known examples of trials that can be, and have been, accused of suffering from the "reasonable availability problem"; fx the AZT, Havrix and Surfaxin trials (Resnik 2003 pp. 247-249, Hawkins & Emanuel 2008, pp. 1-2 & 55-61).

and unpleasant side effects, here the only source of harm is the minor, short-lived pain associated with having one's blood sample taken, and the only present risk is the largely minimal one associated with infection from the needle. On a purely practical level, benefits are similarly meager: the fact that the donors' blood samples are stored in the biobank is very unlikely to lead to any real direct benefits for them. However, these are not the only sort of relevant benefits: it may very well be that the donors achieve psychological benefits from giving their blood sample, in feeling that they are doing something with respect to their disorder, or contributing to research and the furthering of knowledge.[38] Viewed in this light, it may in fact be the case that the harm/benefit profile of the research works in the favor of the donors.

Turning now to the interpretation of unfairness as having to do with the distribution of benefits between researchers and donors, the concern here could be that the researchers will accrue substantial benefits from the donors' sample, in the form of scientific developments and potential monetary rewards following it. In practice, however, it is not obvious that the biobanking of the donors' samples will yield any benefits to the researchers that are large enough for this to be a relevant concern. To explain, let us take a brief look at what will likely happen to any given sample collected, registered and stored in the biobank. It may, or may not, be used in a study on a particular disorder. If so, the sample will likely enter into studies along with those of hundreds or thousand other donors. These studies may, or may not, result in some progress in scientific knowledge. If researchers do manage to glean some new knowledge or insights from their research on donors' samples, this may result in a publication (or, in special cases, maybe even a few). However, it is rarely the case that anything more than this comes out of it.

If we understand exploitation in research as an unfair distribution of benefits – as Wertheimer and many other theorists do – this presupposes that the benefits in question are of a size or nature for this to be a concern. We have established that this is not the case. Hence, on an unfairness-centered account, our case is not one of exploitation.[39]

Some may disagree on this point, and maintain that the case indeed does hold potential for an unfair distribution of benefits (whatever this may be). My response is that if we want to hold that the case is exploitative, it must at least be of the mutually advantageous, rather than harmful, kind. As Wertheimer

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[38] Here it can be argued that this is not a "real" benefit, in the sense that the benefit donors feel comes not from actually getting something out of their participation, but rather from the *illusion* that they do (it would here take us to far astray to engage in further discussions of the value (or non-value) of this illusion (one could for example refer to Robert Nozick's thought experiment *The Experience Machine;* see Nozick 1974, pp. 42-45), so I shall halt this venture for now). Be that as it may, it is common in the literature to recognize psychological benefits of this sort as genuine benefits on par with health benefits – see e.g. Nobile et al. 2016; Kamuya et al 2014; Hoeyer 2010; Busby 2010; King 2000.
On this note, a colleague has put forth the challenge that we should be cautious in accepting and encouraging actions that may provide psychological benefits, but at the same time detract from one's health and welfare. I understand this concern, but disagree that it should result in a wholesale rejection or prohibition of such actions. It would, for instance, discourage against organ donation between close family members: should I decide to donate a kidney to my father in kidney failure, my physical health and well-being may suffer a hit; however this is easily made insignificant to me by the immense psychological benefits I receive from knowing that he will live with a functioning kidney, and for having him in my life for a prolonged period of time.

[39] Now, if benefits to researchers were in fact significantly larger than they are (with the benefit to donors remaining constant), then according to the unfairness-centered account we might have a case of exploitation on our hands. This indicates that from the view of unfairness-centered theories, what is relevant in determining whether our case is one of exploitation is exclusively what happens to the sample and what benefits are accrued from it. However, given the context of international research it would be naïve and myopic to assume that this should be the only relevant parameter regarding the potential exploitative nature of our case – which points to the relevance of including circumstances and vulnerabilities in the discussion, as I do later in this article.

notes, to determine whether this is the case we must look at the transaction's net effect on the alleged exploitee, in our case the donors. As we have shown, in our case the donors are highly likely to benefit more than they are harmed, all things considered. Furthermore, they seem more likely to receive a direct, imminent benefit than are the researchers (in the form of psychological benefits). In terms of their potential exploitation, then, it appears that from the unfairness-as-outcome approach there are no substantial harmful effects to cause grounds for exploitation concerns – and the harmful effects that there may be (e.g. pain from having one's sample taken, or the negligible risk of infection) are, in the big picture, too minor to warrant a genuine moral concern.

However, recall that unfairness as a central element of exploitation may also have to do with not just a certain outcome of a transaction, but also how this has come about – namely, whether coercion, fraud or misinformation has tampered with the exploitee's consent to the transaction. In our case, nothing speaks of coercion, so we shall leave this for now. But what about fraud and misinformation? As we explored earlier, fraud and misinformation in relation to exploitation amount to making B believe something false regarding a transaction, as a means to get B to agree to the transaction, which benefits A. Recall that the donors are informed that *their samples will be used in research on their disorder (and perhaps related disorders), which may down the line lead to insights into how to control and prevent the disorder(s)*. This is not misinformation per se, but it can be argued that the researchers withhold an important piece of information, namely that the insights mentioned are not very likely to come from the individual donors' samples in themselves (but in combination with many other donors' samples), and it is even more unlikely that these insights will have direct consequences for the individual donors' health situation.

This is further complicated by several specific, local features of the case: due to their lack of education, donors may not have a conception of the nature of research (as opposed to that of treatment). When people present themselves as from the medical profession, this is associated with a being a doctor, and this is associated with the possibility of receiving treatment. There is thus a live risk that donors are not fully capable of distinguishing between research and treatment – most importantly with respect to that one "gets something out of" the latter, and not the former (in the form of a diagnoses and/or treatment). Without the crucial distinction between research and treatment, donors may thus be of the conviction that they are agreeing to something else than they are – namely that they are getting a treatment or certain results, which they due to the nature of the research will not. It can be argued that the researchers are not providing false information *per se* – but it seems as an equally grave offense to fail to provide relevant true information, which would correct the misconception, where this information is relevant to the donors' willingness to transact.[40] It is of course an open question (and the answer likely varies from one donor to another and their background preferences, etc.) whether the genuine understanding that they will not receive any treatment from their participation would deter them from participating (or, whether their belief that they will get something out of it is central to their participation): as touched upon, donors may benefit just from feeling that they are "doing something" rather than nothing, or that they are participating in something that will help mankind, if not themselves. But if we suppose that this information is in fact central to at least some donors' decision whether or not to donate a sample, and if researchers

[40] This may be related to the *therapeutic misconception* (Appelbaum et al. 1987). This is a globally observed phenomenon, and as such is not especially associated with developing countries. However, it should be noted that local circumstances in developing countries in general may be far more conducive for this to take place (as pointed out by Hawkins & Emanuel (2008), many languages lack words for important and relevant medical-scientific concepts, and in authoritarian cultures it may be difficult to get subjects to understand that they are really free to not participate, and their health care and other interests will not be jeopardized if they refuse), and thus there rests a larger responsibility to correct for this on researchers operating in developing countries.

purposefully do not disclose or remain vague about this as way of getting donors to consent to donate a sample which they otherwise would not have, then this is unfair and exploitative.

Summing up, we can say the following: on an unfairness-centered account of exploitation, it is not unequivocally clear that our case is one of exploitation. However, there is a possibility of it being so on a certain interpretation of unfairness: in an interesting contrast with other work on exploitation in research in developing countries, the potential for exploitation has less to do with the distribution of *benefits* between the research participants and researchers/sponsors, and more with the *process* of the transaction – namely, the way the decision to participate is formed on the basis of available information. However, it seems that this does not fully exhaust or explain the potential for exploitation in our case: as noted, it may be the case that donors wish to participate even when they are fully aware of the conditions of the transaction (most importantly, that they will not receive any tangible benefits) – and we may still intuitively find this situation to be exploitative. Why? An unfairness-centered account such as Wertheimer's has a hard time answering this, and the reason for this seems to be that it necessarily takes the wrong-making feature of the transaction to lie in the transaction itself (be it the outcome or process). As an alternative perspective, let us turn to exploitation theories that focus on the *circumstances* of a transaction as the wrong-making and defining feature – or in other words, that the wrong in exploitation has to do with how the exploiter takes advantage of the exploitee's circumstances.

4.3. Circumstance-centered theories

We can imagine a situation where a person gives full valid, voluntary and informed consent to a transaction and still benefits, but we would still call it exploitative – however not for reasons related to particular outcome of the transaction. One tragic case that illustrates this is that of what The Daily Mail has termed 'survival sex' (Jay 2016) – women among Syrian refugees in Lebanon who, without access to the job market and thus any other means of sustaining themselves, have to resort to providing sexual favors in return for housing, food or employment; often accompanied by their daughters. Here, the women and their daughters benefit from the transaction (compared to a non-transaction situation, which would likely leave them starving and without a roof over their head); we can assume that they enter into the transaction without being coerced and that they are fully informed about the terms of the transaction (i.e., sexual favors in exchange for some good that they need); however we can also relatively safely assume that they would not have agreed to the transaction had they circumstances been otherwise. This indicates that, *contra* the viewpoint of Wertheimer and related theorists exploitation is a function of the *circumstances* of the transaction, not the outcome.

A note on terminology: the particular way people are in a bad position (and that this bad position is what makes them open to exploitation) is often articulated as "weaknesses" or "vulnerabilities". These words may be deceitful, though: it seems that there is a relevant difference between *being weak/vulnerable* and *being in a weak/vulnerable position* – where it is the latter with which this cluster of theories are concerned (I shall discuss this difference in more detail shortly). For this reason, I shall refer to theories such as the ones presented in the following as *circumstance-centered theories*.

A general formula for circumstance-centered theories may be the following:

> *A exploits B iff A uses B's (unfortunate) circumstances to make him enter into a transaction that benefits A, that B would not have entered into otherwise; and A does so in a morally reproachable way*.[41]

One example of such a theory is put forth by Robert Goodin (1987). Goodin states that the connection between exploitation and harm or benefit is a contingent, not necessary one: it is true that exploited parties often happen to suffer a material loss as a consequences of having been exploited, however this fact is not analytically necessary for them to be exploited. This is because, on Goodin's view, exploitation is about something else than loss with respect to a baseline of benefits or goods. It is taking advantage of some peculiar features of the situation in which exploiters and the exploited find themselves, in a way that violates the specific moral duty not to take advantage in situations where the circumstances prescribe that you are morally bound not to do so (Goodin 1987, pp. 166-167). In this way, exploitation does not concern a certain end state (as e.g. Wertheimer holds), but rather whether there is something morally suspect about the way in which this end state has come about. As Goodin states,

> *"It is not a matter of how things end up at all. It is instead a matter of how you got there. The essence of exploitation must be sought in some characteristic of the process, rather than in some characteristic of the end result.* […] *The wrongfulness […] lies in the act, not the outcome"* (ibid., pp. 181-182).

So what characteristics of the transaction process should we look for to determine whether it is an exploitative one? Here, Goodin employs a game analogy and suggests that exploitative behavior is the antithesis to "fair play" in the given context, i.e. availing oneself of strategic opportunities which are denied to one under the rules and ethos of the game at hand. What is unfair, then, is contextually dependent: there is nothing about acts that make them intrinsically exploitative; it depends on the nature of the 'game' people think they are playing (ibid., p. 183).[42] What makes all instances of exploitation unfair is that it involves playing for advantage where it is morally or normatively inappropriate to do so. One scenario for this to play out is when one party finds himself in dire circumstances, and the other party turns this to his own gain (for example, Wertheimer's unfair surgery case). This is wrong *not*, as Wertheimer holds, because B pays more/receives less (understood broadly) than what he is due according to a fairness baseline (which is the standard price for surgery), but because it is wrong for A to turn B's situation to his advantage in the first place. Occasions for exploitations arise when one party is in an especially strong position vis-à-vis another – e.g. when B is in a bad position and A has the means to help him out. According to Goodin, such circumstances generate a special moral duty and responsibility to protect the weaker, and to not do anything that would constitute taking unfair advantage of those who are particularly sensitive to our actions and choices. It is the violation of this duty – which is laid upon each and every one of us – that constitutes exploitation (ibid., p. 167, 189).[43]

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[41] As will be made clearer below, what makes A's taking advantage of B's (unfortunate) circumstances morally reproachable, and thus qualifies it as exploitation, is closely tied to the moral demand that when we encounter someone in such circumstances, our first instinct should be to help them out of this situation in any manner we can, instead of seeking to procure a benefit for ourselves from their predicament. Several circumstance-centered theories are anchored in this moral demand, and in the case of the Syrian refugees, it seems fairly obvious that we are morally required to help them instead of (or, in a way that does not entail) purchasing sexual favors from them. However, it is my intuition that in cases without such obvious grave circumstances and glaring power asymmetries, this analysis will be less straightforward.

[42] Similarly, there is nothing about circumstances as such that make them intrinsically exploitative.

[43] It may of course be questioned whether such a duty in facts exists, and in that case how it should properly be delineated. For example, exactly how 'weak' does one have to be to invoke that another should not take advantage, and is it a given that being in a bad position makes you 'weak'? These are questions for a further discussion of Goodin's theory, however, and I will not concern myself further with them here.

A related view is put forth by Mikhail Valdman (2009). Valdman states that the deepest wrongness of exploitation "*lies in our moral obligation not to extract excessive benefits from people who cannot, or cannot reasonably refuse our offers*" (Valdman 2009, p. 1). Exploitation happens when B is in a position where she cannot reasonably refuse A's offer, and where A uses this leverage to extract excessive benefits from B.[44] Wrongly exploiting someone requires that one wrongs her *by* exploiting her – in other words, by engaging with people the way just described, we wrong them. For the purposes of this paper, I shall focus on the 'reasonable' element of exploitation in Valdman's account (for reasons that will made clear below, I disagree with Valdman's claim that excessiveness of benefits is a necessary condition for a transaction to be exploitative).

So, what does it mean to be unable to reasonably refuse an offer? Valdman offers that this is the case when one faces *unacceptable non-transaction costs,* i.e. where not engaging in the transaction severely harms one's basic personal interests. This is calculated in terms of *urgency* and *monopoly*, more specifically a combination of the two: when you find you yourself in a situation where you have an urgent need with respect to your basic personal interests, and only a monopolist (broadly construed)[45] can satisfy this need, you are unable to refuse any offer he might propose (Valdman, pp. 9-10).[46] To illustrate this point, Valdman sets up his *Antidote case* (Valdman 2009, p. 3):

> B is hiking in a remote forest, and is bitten by a poisonous snake. His death is imminent. Fortunately, A comes by with the antidote and offers to sell it to B for no less than $20,000, even though the retail price is $10. B would rather lose his money than his life, and accepts the transaction.

While this exchange is clearly consensual and mutually beneficial, it is also clearly exploitative.[47] The reason for this is, on Valdman's view, that B is in a situation that is not only highly unfortunate, but also threatens to severely harm his basic interests; and that A takes advantage of the fact that he is B's only hope.

As noted in at the beginning of this section, however, the difference between *being weak or vulnerable* and *being in a vulnerable situation* is not always clearly articulated in this type of theories. In Valdman's Antidote case, for instance, we might, through our associations to how a poisonous snake bite usually affects people, be led to latently believe that the hiker is perhaps already suffering effects of the snake's poison, interfering with his mental capacity – making him vulnerable in the usual sense of the term, and not merely placing him in a vulnerable situation.

To clarify this point, I offer the following refined version of Valdman's antidote case. This will serve as an illustration of the type of cases that, I think, Valdman and Goodin (and other circumstance-oriented theorists) are concerned with – that is, cases where it is the particular *circumstances* (and not inherent characteristics of the people in them) that offer grounds for exploitation:

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[44] By claiming two elements – 'excessive' and 'unreasonable' – as necessary for exploitation, Valdman himself distances himself from the view of Goodin (who, in the words of Valdman, holds that "exploitation's wrongness lies in the opportunistic use of people's vulnerabilities"; where vulnerabilities refer to an agent's circumstances). On Valdman's view, the benefits extracted from a transaction need to be excessive, and not merely come out of a situation where one party could not reasonably decline the transaction. However, as Valdman also takes exploitation to be a feature of circumstances of a transaction, and not of the outcome, it makes sense to place him in this category alongside Goodin.

[45] A monopolist need not be someone who has actually cornered the market for some good or service; he just has to have done it vis-a-vis the party in question.

[46] As with monopoly, we should understand urgent needs broadly, to include what is needed to live a decent life; not just to avoid misery or death.

[47] Here, Wertheimer and Valdman are in agreement that the moral wrongness of exploitation often has to do with something else than harm or consent.

> Imagine a wealthy, intelligent, educated bodybuilder who unfortunately happens to fall down a deep hole in the middle of a deserted forest, with no possibilities of utilizing his strength or education to get himself out. With no help from outside sources, he is left there to starve to death. Luckily, an off-track jogger discovers our bodybuilder in the hole, and offers to help him out – on the condition that he gives her half his fortune and helps her build a house.

Would we not say that our poor bodybuilder is not weak or vulnerable, but merely in a very unfortunate situation? I think yes. Would we not say that the bodybuilder is being exploited by the jogger, and that the jogger has the option to do so precisely because the bodybuilder finds himself in this particular situation? I think yes.

Before moving further, a few comments on my decision to place Goodin and Valdman in the same category. By claiming two elements – 'excessive' and 'unreasonable' – as necessary for exploitation, Valdman explicitly distances himself from the view of Goodin (who, in the words of Valdman, holds that *"exploitation's wrongness lies in the opportunistic use of people's vulnerabilities"* (Valdman 2009, p. 1), where vulnerabilities refer to an agent's circumstances). On Valdman's view, the benefits extracted from a transaction need to be excessive, and not merely come out of a situation where one party could not reasonably decline the transaction. So we see a difference in what the two theorists take to be the central moral wrong of exploitation: for Goodin it is to play for advantage where you are morally bound not to do so, and for Valdman it is to extract excessive benefits from those that cannot reasonably refuse our offers. Nevertheless, as both authors take exploitation to be a feature of the circumstances of a transaction, and not of the outcome, it makes sense to place them both in the family of theories that I have termed circumstance-centered theories of exploitation.

Summing up, circumstance-centered theories take the wrong-making feature of exploitation to be that the exploiter takes advantage of the fact that another party – notwithstanding however resourceful they might be – find themselves in a particular situation where they have their back against the wall, in order to get them to engage in a transaction that benefits the exploiter or his interests (excessively or not). This is a moral wrong because of the certain moral duty that arises precisely when we recognize we are in a particularly powerful position vis-à-vis someone else because of their particular circumstances, to not engage in transactions that take advantage of this fact.

4.3.1. Application to the Pakistan case

Applying these considerations to our case, it seems that two conditions must be met for it to be one of exploitation: 1) the donors must find themselves in a bad situation, and this in such a way that they have no reasonable choice but to engage in the transaction suggested by the researchers (i.e., donating a blood sample), and 2) the researchers must use this fact to get the donors to agree to donating a blood sample (thereby violating the duty to not to take advantage of those who are particularly sensitive to their actions). Let us explore these in turn.

First, we can say that it is not incorrect to say that the donors are in a bad position generally speaking: as stated in the beginning of this paper, they are in circumstances where they find it difficult and stressful to cope with their disorder under circumstances of few individual resources and poor medical infrastructure. Being approached by the researchers offers a promise of much welcome medical attention, which they

otherwise lack. By giving a blood sample, they will receive attention to the disorder that has their family afflicted, and will thus likely be highly inclined to agree to this transaction. But is it the case that they have *no reasonable choice* to decline the transaction, that is, that their non-transaction costs are unacceptable? This does not seem to be so: the researchers are not physically coercing them into giving a sample, and they are not threatening to make them any worse off should they decline to give samples. Furthermore, the donors will not themselves suffer any reduction in their welfare by declining the transaction. If we compare this case with Valdman's antidote case, it becomes clear that donors can easily walk away from the transaction in a way that the snake bite victim cannot: by declining, donors do not stand to lose anything substantial in terms of life, health or basic welfare. In other words, they do not, in Valdman's terms, have any unacceptable non-transaction costs. If we take unacceptable non-transaction costs to be a prerequisite for exploitation – as circumstance-centered theories of exploitation usually do – by not having such, it seems that the donors are not in a position where they might be exploited.

But we may be moving a bit too fast here. It is not a given that unacceptable non-transaction costs are adequately or properly cast in terms of severe harms to basic personal interests or welfare, such as life or health. There may be other factors at play that make the non-acceptance of the researchers' proposal unfeasible for the donors. Recall that, as Valdman points to, unacceptable non-transaction costs also has to do with *monopoly*, and further that a monopolist may rightfully be conceived of as having merely cornered the market with respect to the party in question. The donors in our case are situated in a remote rural area, with very limited access to any medical care (due to both distance, infrastructure and economic resources) – and are then approached by the team of researchers who offer the prospect of medical attention, 'no strings attached', on a silver platter. Donors may likely view this as a unique opportunity to cash in on the hope of receiving any sort of medical attention – who knows when a team of medical professionals will happen upon their remote village again? – and they will thus be very hard pressed to comply. We may say, then, that it still holds that the donors do not have unacceptable non-transaction costs from a purely objective standpoint; but from a subjective angle (i.e., their own) they might be in a position where consideration of their personal hopes and goals makes it, if not unacceptable then at least very undesirable, to decline.[48] Here, it can be argued that the problem is not that the non-transaction costs are high, but that the donors *think* that they are – if, for example, they falsely believe that donating a sample will result in a benefit in form of a cure. This would then be a case of exploitation based on false beliefs. However, the donors may also benefit from merely receiving the medical care and attention that comes with donating a sample (recounting the history or their family disorder, receiving sympathy, etc.) In this case the donors may be right to believe that this is not something that will happen again any time soon (as researchers, indeed, rarely come by their village), and view the researchers' visit as a unique opportunity that they cannot forego. To sum up, there may in practice be grounds for exploitation here; however it is not unequivocally clear that this is so.[49]

Second, to determine whether the researchers are exploiting the donors on a circumstance-centered account, we must look at whether they violate their moral duty vis-à-vis the donors – in Goodin's terms, to not play for advantage where you are morally bound not to do so, and in Valdman's terms, to not extract (excessive) benefits from those that cannot reasonably refuse our offers. As we have just established, we cannot unequivocally conclude that the donors *cannot refuse* the researchers' offer, so we can rule out that it is unequivocally the case that they exploit in this (Valdman's) sense. But as we saw

[48] Some may object that this is not an unacceptable non-transaction cost, but rather (or merely) the possibility of a very high gain – which does not have the same impact on the potential exploitative nature of a situation.
[49] In the next section I will discuss why and how these circumstances may still be problematic with respect to exploitation.

with Goodin, this moral duty towards others further implies special attention to not playing for advantage against those persons vis-à-vis whom you are in a stronger position, and not breaching the ethos and rules of the game people think they are playing. Especially the latter quickly becomes an issue in the context of the obligations of research vs. those of treatment – do research subjects always know which 'game' they are participating in? This issue has been discussed at length in the literature, especially in relation to therapeutic misconception,[50] and appears to be relevant in our case as well. It may be rightfully claimed that formally, the aims and obligations of research and treatment *are* different – in the words of Wertheimer,

> *"The aim of research is to seek generalizable knowledge. By contrast, the aim of personalized medical care is to advance the health of the patient […] and the treating physician has an obligation to pursue that goal"* (Wertheimer 2001, p. 226).

This would indicate that there are different sets of moral obligations attached to each of the two practices – and to put it in the words of Goodin, there seems to be different responses to what constitutes 'fair play' in the respective contexts. For example, if a patient presents in his doctor's office with a serious (but not life-threatening) rare illness, and the doctor refers him to a researcher investigating precisely this disease, it is 'fair play' for the researcher to take a main interest in securing samples from the patient as a means to further his own research project, and a lesser interest in curing the patient. However, this would *not* be 'fair play' if done by the doctor in his office, if we imagine that he happens to be working with the researcher in investigating the disease in question – in this case the main interest should still be in curing the patient.

In our case, it seems there is at least a risk that the donors *think* that they are playing a different 'game' than the researchers do: they think they are to receive a treatment, when this is not so (this is often ascribed to the effects of illiteracy and lack of education in complicating clear communication regarding treatment vs. research). And as Valdman relevantly points to, the *blameworthiness* of one's potentially exploitative actions toward another "*partly depends on what he knew or should have known about [the other's] ability to refuse one's offer"* (Valdman 2009, p. 13), but also that *"these epistemic considerations are not relevant to whether A wrongly exploited B"* (Ibid., p. 13). I think Valdman is right in his first statement, but I disagree with his latter point: if I know that someone else has misunderstood facts of a certain situation, and I use this to my advantage over said person, I am clearly breaching a moral duty and am blameworthy. There may, then, be something to be said for the researchers' epistemic state with respect to whether their conduct is exploitative. If the researchers know that the donors a) are likely to view declining their offer as unacceptable and b) think they are receiving something from participation though they will not, it would seem that this would qualify as a situation where it is morally and normatively inappropriate to play for advantage – by using this knowledge about the donors' epistemic state to secure their participation.

The conclusion we arrive at, then, is that strictly analytically speaking, on a circumstance-centered account of exploitation our case is not, conclusively, exploitative. Nonetheless, one might still have intuitions that point in the other direction – namely that there is something suspect about the relation between the characteristics of the donors and their situation on the one hand and of the researchers and their interaction with the donors on the other; and that our intuitions about exploitation concern this. We just established that circumstance-centered theories cannot fully explain this – however, of the three

[50] Therapeutic misconception *"occurs when a research subject fails to appreciate the distinction between the imperatives of clinical research and of ordinary treatment, and therefore inaccurately attributes therapeutic intent to research procedures"* (Lidz & Appelbaum, 2002, p. V-57).

families of theories examined, it seems that this view comes closest to capturing our intuitions about the potential wrong-making features of our case. I suspect, then, that the reason the circumstance-centered theories are not satisfying in this regard is that they are not nuanced enough in their view of vulnerabilities.

5. 'Vulnerabilities' – revisited and refined

So far we have employed the dominant theories of exploitation to analyze whether the Pakistan case is one of exploitation, and if so, which features of the case that may be grounds for this. For all the theories applied, the general upshot is that our case is not exploitative. Circumstance-centered theories come closest to targeting our intuitions about the case, but it still seems that there is a lot of way to go.

I suspect that the reason for this is that this family of theories have the right approach – looking at the specific circumstances of a transaction, rather than the outcome, for grounds for exploitation – but their accounts for what constitute vulnerability are nowhere near nuanced or fine-grained enough to capture exactly *how* and *why* the circumstances in our case provide grounds for exploitation. To correct for this, it might be helpful to turn to the body of recent work that has – precisely – criticized the notion of vulnerability in exploitation in research ethics as being far too broad and coarse-grained, and put forth alternative nuanced accounts.

These alternative accounts have in common that they instead advocate for a pluralistic view of vulnerability. This should be understood in the sense that vulnerability is not one single, easily identifiable and describable phenomenon; rather, individuals may be vulnerable in different ways in certain situations and with certain people. What makes them vulnerable in all of these contexts, however, is that the combination of their own characteristics and those of the circumstances and other individuals in it have a certain adverse effect of their decision-making capacity.

5.1. Guidelines on vulnerability

Several guidelines for ethical research on human subjects address the issue of vulnerable groups, and stress that such groups – due to certain characteristics and circumstances – are more easily exploited in research, and thus require extra, special protections. As examples, The Council for International Organizations of Medical Sciences (CIOMS) states that

> *"Vulnerable persons are those who are relatively (or absolutely) incapable of protecting their own interests. More formally, they may have insufficient power, intelligence, education, resources, strength, or other needed attributes to protect their own interests"* (CIOMS 2000, guideline 13),

and the Belmont Report identifies vulnerable individuals by "*their dependent status and their frequently compromised capacity for free consent"* (U.S. National Commission 1979, p. 20).

The aim of these guidelines is laudable – nevertheless they have been widely criticized in their approach to vulnerability on several tenets (see Kipnis 2001, Hurst 2008, Luna 2009); most importantly in that they mistakenly take what has been termed a "subpopulation approach" to vulnerability, defining and labeling certain groups as vulnerable in virtue of certain characteristics, and further claiming that these particular characteristics in themselves cause a general deficiency in decision-making capacity. We see this e.g. in the CIOMS guidelines, where those who are vulnerable are, among others, the illiterate, uneducated and resource-poor. It seems, however, that this line of reasoning commits the fallacy of equating membership of group X with a general decision-making impairment – a connection that does not hold up when subjected to the harsh light of reality: there is nothing about being (e.g.) poor, illiterate or uneducated *as*

such that impairs your capacity to make decisions. As commentators have rightly noted, such an approach is much too simplified on a theoretical level, and may be highly problematic and stigmatizing on a practical level.

When we identify certain groups as vulnerable in virtue of particular characteristics, we conceive of being vulnerable as a fixed label (Luna 2009) – if you meet the criteria for being in group X, you are vulnerable; period. This overlooks the reality that not everyone is vulnerable to everyone and at all times; but usually only to some people and in certain respects and situations (as an example we can imagine an intimidating and extremely self-confident CEO of a large multinational company with an reputation for firing employees for minor mistakes, who becomes compliant and deferential only in the presence of his domineering wife). As Levine et al. note,

> *"[a]n individual's needs for special protection depend not solely on that person's inclusion in a group, but importantly on the particular features of the research project and the environment in which it is taking place"* (Levine et al. 2004, p. 47)

A labelling approach, as the one taken by the 'subpopulation view', overlooks this fact, that vulnerability is highly contextual and situational, and thus suggests a much too simplistic answer to this complicated and complex problem. It may be argued that the guidelines commit the fallacy of not properly distinguishing between *being vulnerable* and *being in a vulnerable situation*, discussed previously in this paper. This is problematic not only on a theoretical, but also an ethical-practical level: merely listing groups that are vulnerable does not shed any light on *why* and *how* these individuals are vulnerable, or, effectively, what can and should be done to accommodate it. As Zion et al. correctly note, *"medical research takes place within a complex web of power relations"* (Zion et al. 2000, p. 615). If we merely look to the 'fixed' characteristics of a certain group for vulnerabilities, we not only overlook the fact that research situations are often highly complex and influenced by context, we also remove focus from certain aspects of the research protocol and setting that may generate vulnerabilities with this particular group, that it may not with other groups (for example, a standard informed consent form for a clinical study containing information in standard scientific language may be adequate for an educated research participant who understands the level of detail and information, but not for one who does not – in this situation only the latter individual is vulnerable)[51].

5.2. Alternative accounts of vulnerability

In response to these theoretical shortcomings, several authors have recently proposed alternative accounts of vulnerability, that take a more nuanced, dynamic and relational view. A general feature of such accounts is that they explicitly oppose the labeling approach to vulnerability (as manifested in the ethical guidelines reviewed above), and in contrast to this, view vulnerabilities as something inessential, and as a function of the relation between the specific situation and the specific people in it (and their characteristics): people may not be vulnerable in an 'everyday' sense, but find themselves in a certain situation that make them open to exploitation form certain others. On such a view, then, we cannot identify exploitation merely by looking to groups that we deem vulnerable, but have to take into account the entirety of the situation and circumstances, in a way that must necessarily be more sophisticated and fine-grained than the circumstance/vulnerability views offered by e.g. Goodin and Valdman.

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[51] Kenneth Kipnis also notes that "in the minds of many investigators the paradigmatic research subject remains more or less a mature, respectable, moderately well-educated, clear-thinking, literate, self-supporting U.S. citizen in good standing." (Kipnis 2001, p. 1). Where e.g. the standard procedure for informed consent may be adequate for such individuals, it may not be for individuals who do not fulfill these criteria.

However, what these theories helpfully contribute with respect to nuancing the concept of vulnerability, they lack in explicating exactly *why* such vulnerabilities are problematic, that is, exactly what the causal link between vulnerability and exploitation is. Such accounts rightly and timely show the highly contextual nature of vulnerability, but to a bigger or lesser extent fail in demonstrating exactly what it is that turns a certain situation into an exploitative one. I think that what is tacitly assumed by these accounts is that vulnerabilities are constituted by a *contextually dependent impaired decision-making capacity*, and it is this impaired decision-making that opens avenues for exploitation. People are open to exploitation (i.e. vulnerable) when the interaction between their characteristics and certain features of the situation and the people in it impairs their decision-making, and in effect the efficacy of their consent.

Lack of analytical acuity aside, I believe these accounts offer valuable and important insights into just how complex real-world cases of exploitation can be, with respect to what it is that may impair (in many cases otherwise sane, rational and resourceful) individuals' capacity for decision-making. In the following, I thus proffer such suggestions for more nuanced views of vulnerability as just that: alternative suggestions for what may make individuals vulnerable with respect to exploitation in certain situations. Where warranted, I will attempt to qualify and exactly how these vulnerabilities impair individual decision-making, and stress that this is what enables exploitation. I will then demonstrate how such alternative accounts of vulnerability elucidate features of the Pakistan case that are problematic with respect to exploitation, which stay hidden from view if we merely apply the standard theories of exploitation. This will be a somewhat lengthy endeavor, but I believe it is warranted.

In explicit opposition to the labeling approach, Florencia Luna (2009) offers what she terms a 'layered' notion of vulnerability: it is not that certain groups are essentially or *per se* vulnerable, but rather that they may be *rendered vulnerable* in certain situations by certain specific societal, cultural or structural factors: due to the specific situation and their own characteristics they *acquire certain overlapping layers of vulnerability* (Luna 2009, p. 122; 128-129).

I think that what Luna means by 'being rendered vulnerable' is that an individual may find him- or herself in a situation where certain societal cultural or structural factors impair his or her capacity to make decisions. Where an individual 'acquire certain overlapping layers of vulnerability', I believe we can take this to mean that the individual's decision-making capacity is impaired on one or more levels. In this account of Luna's theory, then, I advocate that we understand her mentions of 'vulnerability' as 'impairment with respect to decision-making'.

Responding to the notion that women are sometimes considered vulnerable *simpliciter,* Luna illustrates her conception as follows:

"[b]eing a woman does not, in itself, imply that a person is vulnerable. A woman living in a country that does not recognize, or is intolerant of reproductive rights, acquires a layer of vulnerability. […] [A]n educated and resourceful woman in that same country can overcome some of these consequences of the intolerance of reproductive rights; however, a poor woman living in a country intolerant of reproductive rights acquires another layer of vulnerability. […] [A]n illiterate poor woman in a country intolerant of reproductive rights acquires still another layer" (Luna 2009, pp. 128-129).

In this way, any individual stands to acquire a number of overlapping layers of vulnerability, depending on the given situation and circumstances. If the situation, or a number of variables in it, changes, she may no longer be considered vulnerable – for example, in a situation where there is crucial information to be read, being illiterate can make you instantly vulnerable; however this changes the second there are instructive illustrations provided, or a literate individual offers to read aloud for you. In this way, the concept of vulnerability is a relational one, in that it concerns the relation between a person or a group of

person and the circumstances/context. Layers of vulnerability (or, on my reading, impairment with respect to decision-making) appear as a result of the *interaction* between individuals' particular circumstances and particular characteristics. [52] According to Luna, this richer notion of vulnerability allows us to think of vulnerabilities as a function to economic, social and cultural conditions, and forces us to recognize that such conditions may invoke several different layers of vulnerabilities, operating on different levels and affecting different aspects of an individual's life. Merely focusing on 'vulnerability' as an umbrella category will not properly highlight nor accommodate them.

In a similar vein, Kenneth Kipnis (2001) suggests that we should understand vulnerabilities in the research context in a special sense, namely as *"those special circumstances of the [research subject] that call into question the efficacy of consent in effecting the permissibility of research"* (Kipnis 2001, p. 2.), and further states that someone who is vulnerable in the 'everyday', colloquial sense (e.g. blind people, who are characteristically less able to protect themselves), may not be vulnerable in a research context. What Kipnis does not explicitly state, but that I think we can reasonably infer from the rest of his account, is that his latter claim also works *vice versa*: a person who is *not* vulnerable in the 'everyday', colloquial sense of the term, may, in fact, be a vulnerable research subject. Vulnerability is not something inherent or essential in certain individuals, but can rather be described as some characteristic of the individual in interaction with certain circumstances that may make her vulnerable to certain other people. To give substance to this notion, Kipnis offers a taxonomy of vulnerability;[53] identifying six different dimensions on which individuals may be vulnerable with respect to their agreement to participate in research, and consequently the permissibility of such research: cognitive, juridic, deferential, medical, allocational, and infrastructural.[54] The three former are of special interest with regards to our case, so I shall leave the others for now.

Of the six types, *cognitive vulnerability* is the one most commonly recognized in the research ethics literature. It refers to an individual's lack of capacity to deliberate and decide about participation in a study, and may be indicated by individual characteristics such as immaturity, dementia and mental retardation; but also educational deficits and unfamiliarity with the language (Kipnis 2001, p. 5). As Kipnis notes, vulnerability is present here precisely because the measures ordinarily taken to ensure that the individual is adequately informed will not do in the face of such circumstances.

Juridic vulnerability refers to the formal authority relationships that often characterize social structures, e.g. children who are under the authority of their parents, and certain third-world women who may be legally subject to their husbands. Again, such circumstances do not make individuals vulnerable *per se* – rather, the concern is that the juridic fact of their subordination to another may influence the validity of their consent, as it may merely be a reflection of the wishes of those in authority.

Deferential vulnerability is closely related to juridic vulnerability, as it is to be viewed as the *"deferential patterns [that are] subjective responses to certain others"* (ibid. p. 6); often as a psychological effect of the objective features of the formal hierarchical context within which the individual finds herself. This can be exemplified by the (generally) intuitive obedience to a police officer, or the general tendency to comply with a doctor's orders. On closer scrutiny, however, it seems that this type of vulnerability is not

[52] Luna does not address exploitation as such, but as I shall show imminently, Hallie Liberto (2014) shows how her conception of vulnerability, one very similar to Luna's, paves the way for exploitative situations.
[53] It is worth noting, as Luna does (and with which I agree), that these six dimensions hardly exhaust reality and the myriad ways we humans may be vulnerable to each other (Luna 2009, p. 135). However, Kipnis' taxonomy provides a helpful starting point to addressing those 'subtler' types of vulnerability that may be present in many interpersonal relationship and research contexts alike.
[54] These are detailed in Kipnis 2001, pp. 4-9.

only present in the context of explicit power asymmetries (such as with police officers and doctors), but may also be present in informal social relationships – as is the case with e.g. peer pressure (for example, the willingness for the new girl at school to accept a cigarette from one of the popular girls, even though she does not smoke). The vulnerability here is the individual's *"readiness to accede to the perceived desires of certain others notwithstanding an inner reticence to do so"* (ibid., p. 6).[55] As the above examples show, deferential vulnerability may emerge in any social relation, but is more easily identified where there is already a juridic relation to 'flag' it. In settings where this is not the case, this type of vulnerability is much more easily overlooked, however no less powerful. As an example, Kipnis mentions third-world women who may find it hard to turn down requests from men. This particular sort of vulnerability is only identified if one knows where to look; that is, is aware of the particular relevant features of the interaction between a situation and the characteristics of people in it – in this case, that it is a cultural norm to behave in a certain way towards certain people – which, without this background knowledge, may make this simply appear as common friendliness and cooperation.

Now, even though Luna and Kipnis do not explicitly, or at any length, relate their conceptions of vulnerability to exploitation, it should nonetheless be fairly clear from my discussion of their theories how their conception(s) of vulnerability might, in many instances where it is present, pave the way for exploitation. To further corroborate the connection between vulnerabilities in this alternative sense and exploitation, I will include the account of Hallie Liberto (2014).

Liberto takes as her starting point Valdman's claim that for exploitation to be wrongful, it must be that the exploitee has no reasonable way of refusing the offer, and that this requires that one has an urgent need that only a monopolist can satisfy (we saw this in the Antidote case, above). In opposition to this claim, Liberto maintains that it is *not* a necessary condition to have no *de facto* reasonable choice to engage in a transaction in order to be wrongfully exploited in that same transaction. In other words, an individual can have all the reasonable options in the world to walk away from a transaction, yet, should she choose to engage, we may still say that she has been exploited. How is this so? Liberto responds to this by offering a modification of Valdman's account of what it means to be vulnerable, i.e. to have no reasonable choice to transact: it may, in fact, be *objectively* reasonable for the potential exploitee to walk away from a transaction, but *"an alternative might be rendered unreasonable in virtue of a strongly held conviction on the part of the exploitee that his or her options were unreasonable"* (Liberto 2014, p. 622). In other words, it is not (necessarily) the case that the potential exploitee does not know that they have a certain reasonable option available, but rather that he or she has a (true) conviction that putting this option into effect comes with certain social and psychological costs so high that selecting this option is effectively unreasonable.

As helpful illustrations of this point, Liberto offers several cases, of which I shall present two.

> *Poor Student Renter.* A poor college student (let us call him Travis), moves from a bad neighborhood to his college town and seeks an apartment for the academic year. The landlord has learned to recruit exactly this type of college students who are used to living in rough conditions, as it allows him to not put in the amount of money and upkeep into the apartment as he normally would, but still charge the same rate as for everybody else. Travis has, on paper, many reasonable options available to him – he could be comparing apartments; he could demand better treatment from the landlord – but due to his

[55] Another way to state this is the following: it influences the *value* of options who suggests or endorses it. If an individual has the choice between A and B, is an admirer of person X, and person X speaks fondly of A; this attaches a certain subjective social and psychological value to A.

> background and lack of experience he does not know that he is getting a bad deal, and he does not know how to go about making rightful demands from his landlord. He could also ask his classmates for advice on how they negotiate in such situations, but since he is already feeling insecure about his inferior social status, he wants to avoid this additional embarrassment. In effect, the landlord continues to charge Travis too much for a badly kept apartment, and Travis continues to pay this unfair rate.
>
> *Date Rape.* A male college student (let us call Mike), lures a female college student (let us call her Fiona) away from a living-room house party and into an adjacent room, and forces himself on her. Mike knows that Fiona has only recently been admitted into the social group and is still relatively unknown to his friends and housemates, and knows that she still worries that she might face rejection from the group. Additionally, Fiona knows that there is a college culture in which it is presumed that women who drink at house parties and wear short dresses like the one she happens to wear tonight are interested in sexual activity; furthermore she knows that several popular college athletes acquainted by Mike and his housemates have been accused of sexual misconduct, so Mike and his housemates think particularly ill of women who make this sort of accusations. For these reasons, Mike feels confident that Fiona will not scream for help, or make any sort of fuss after the fact. Fiona both verbally refuses and physically resists, but Mike does not prevent her from screaming for help from the other partygoers who are within earshot. Fiona does not scream for help, even though there is ample time and occasion throughout the course of the rape, nor does she report Mike's conduct (Liberto (2014), pp. 623-625).[56]

In both these cases, the victims (Travis and Fiona) have several reasonable options available to them to prevent or stop the unfair treatment they receive. However, the combination of several other features of the situation and environment add up in a way that these options come with subjectively unbearable costs for the victims. What makes the perpetrators' actions wrongful (and, as I shall argue shortly, qualifies them as exploitation) is that they count on features of their victims' psychology and environment to hold them fixed in the belief that their other options are untenable.[57]

These cases should make it clear how Liberto's account relates to the vulnerability accounts just reviewed: vulnerability and the resulting openness to exploitation is largely a result of the particular calculation that contains the specific characteristics of 1) the exploitee, 2) the situation and 3) the exploiter, and the interaction between these three elements – more specifically, that this combination impairs the decision-making ability of the exploitee with respect to her options. Characteristics of the exploitee in interplay with her situation makes the refusal of the exploiter's offer not unreasonable or impossible (in the sense we usually understand it), but associated with other harms or stressors that add up in a way so as to rendering the refusal unreasonable according to the exploitee's convictions.[58] The

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[56] Interestingly, it would seem that the wrong in these particular cases can be captured by Goodin's theory of exploitation: that the central wrong of exploitation is to play for advantage where one is morally bound not to do so. It could be fruitful for Liberto to supplement her opposition to Valdman's theory with considerations of how that of Goodin may complement her own account.

[57] It may be argued that the two cases are different in the following way: in the first case, the exploitee does not properly grasp his options to get out of the situaion, whereas in the second she does, but her assessment of their consequences makes her refuse them. Still, the cases are similar in that both victims' ability to do something about their situation is impaired by the social and structural environment, but in Travis' case this is related to the ability to make the choice, whereas in Fiona's it is related to its consequences.

[58] This is open to another interpretation: the exploitee chooses the best option given her circumstances, but the reason that her options are as such is because someone else has provided them with an unfair option set.

exploitee objectively has all reasonable choice to refuse the transaction, but due to a particular combination of her background characteristics and convictions (psychological, cultural, institutional, social, …) combined with features of the situation, this option strikes her as untenable. What are de facto reasonable choices or alternatives for the individual may be constrained by her circumstances and convictions – or, while choices and alternatives may look reasonable at first sight, once all features of the situation are considered, they are not. This means that exploitation can occur in practice even when the exploitee has, theoretically, reasonable alternatives. In this way, exploitation may not only be a result of being in a situation such as the hiker in the antidote case, but may also come from being in a situation where all reasonable alternatives come attached to a perceived significant inconvenience or burden on behalf of the exploitee. As Liberto formulates it, *"a necessary condition on being the victim of wrongful exploitation is [that] all of the reasonable alternatives to the victim are attached to unjust burdens or hassles, and so cage the exploitee"* (Liberto (2014), p. 628, note 4).

Liberto's account instructively points to the many potential complexities in cases of vulnerability and exploitation – most importantly, it shows that real-life cases and what makes them exploitative hardly ever only concern A and B and their mutual transaction as an isolated phenomenon (many other exploitation theories employ this simplistic template), but also the surrounding circumstances and the characteristics of the relation between A and B (and perhaps even other agents). In this way, Liberto's account can be taken to be a pluralist account of vulnerability and exploitation: vulnerability can stem from various matters such as impaired decision-making (e.g., false beliefs about relevant facts or options; impaired reasoning), or being faced with monopoly or an unfair option set – matters which are highly contextual. Exploitation is not reducible to one of these features; each of them (or a combination) can suffice.

In order to fully account for how and why vulnerabilities in Liberto's sense lead to exploitation, I offer the following qualification of her theory: exploitation is taking advantage of the fact that you know that the exploitee (falsely) believes that her options are constrained; fails to have relevant beliefs about her options; faces monopoly; or faces an unfair set of options. One can be said to exploit when one knowingly takes advantage of someone with certain characteristics being in a certain situation where they are not inclined to reject one's offer – when one knows that the other is in a particular social and circumstantial 'cage'.[59]

5.3. Application to the Pakistan case

Let us now see how these meditations on a more nuanced conception of vulnerability may elucidate the nature of potential exploitation in our case. At first blush it seems that, in comparison with the requirements other exploitation theories stipulate, the donors in our case are not in a position where they would typically be open to exploitation. Their case is not a *Snow Shovel* or *Antidote* case (see above). Donors are, for all practical intents and purposes, free to walk away, i.e. to choose whether to donate their sample or not: if they decline, they will not be made worse off with respect to their health or other relevant aspects of their wellbeing, and they will not meet any repercussions from the researchers. Nonetheless, it seems that there are several features of the case which, in the light of our recent discussion

[59] Liberto does not herself formulate a full-fledged definition or criterion of exploitation as such; she merely demonstrates how we need to reformulate 'vulnerabilities' to satisfactorily account for a number of cases of exploitation. Nonetheless, I think that she would agree with my development of her theoretical stance into an actual criterion of exploitation – e.g. in the *Date Rape case,* it seems that Mike *exploits* Fiona because he knowingly *takes advantage* of her psychology and situation for his own benefit.

of different layers and types of vulnerabilities, appear as possible constraints on the donors with respect to their decision-making and thus with respect to the potential for exploitation.

First, there is a risk that the donors, due to their illiteracy and low education, suffer from deficits in understanding of the details of the research and unfamiliarity with the language; elements of what Kipnis terms cognitive vulnerability. It is recognized that these shortcomings are common in developing countries; however it is also rightfully recognized that illiteracy and low education do not in themselves constitute a lack of valid and proper decision-making capacity, and thus we should not take these to be vulnerabilities per se. But the donors may be said to be cognitively vulnerable in a different albeit related sense: lacking the proper knowledge of the difference between treatment and research, donors may envision potential benefits resulting from their participation, and knowing that researchers do not stumble upon their village every day, they may fear missing out on certain benefits should they say no. Note, however, that this can even be the case if they *are* aware that they will not get anything out of the research: studies have shown that even people who are well educated engage in this sort of reasoning (Wadmann & Høyer 2014, Kass et al. 1996, Dixon-Woods et al. 2007, Nobile 2016).

Second, also playing a relevant role is the hierarchical family structures present in this context. Large parts of rural Pakistan are characterized by hierarchical systems in both the private and public spheres. Longstanding cultural traditions and religious beliefs take the family to be the central moral unit, setting out clearly defined power structures within the family unit (Moazam 2000); placing authority for decision-making with other family members besides the individual(s) whom the decision concerns. Hence, it is not uncommon and also legally legitimate for women to have decisions made for them by their husband or their father, or for family elders to decide on behalf of their entire family. This means that certain individuals in our donor population may be at risk of being juridically vulnerable – for example if a woman does not want to donate samples, but is powerless in the face of her husband's authority to decide on her behalf. She does not voice her complaint of fear of repercussions, and her consent is thus merely a reflection of the wishes of the holder of authority.

Third, there are yet other culturally specific factors related to authority that may work in a way so as to impair the donors' decision-making (or at least significantly influence the way they view their option set) with respect to research participation. As we saw in the case description, donors often thought of the researchers as medical doctors, and/or associated with the medical profession and its standards. In Pakistan, a country that places weight on social hierarchical structures and systems, there is a general respect for and intuitive obedience to those that are highly educated, especially if oneself has a lower level of education. Furthermore, the profession of a doctor is regarded as highly respectable; imbuing representatives with elevated, almost divine, insights and authority. As Farhat Moazam writes,

> "[*Reverence and respect toward physicians is due not only to their knowledge and scientific expertise but also to the historical position accorded to the art and science of medicine in Islam. The privileged position of physicians is derived through a historical understanding of the healer as an instrument of divine mercy."* (Moazam 2000, p. 31).

This places an extraordinary authority on doctors:

> *"The "doctor sahib[60]" […] is expected to direct rather than just facilitate medical management. […] Interaction with a physician thus takes the form of recourse to an authority figure and not merely a consultation with a medical expert."* (ibid., pp. 28-31).

Now, if donors believe that the researchers are doctors, they are likely to accord this sort of reverence and authority to them, and to following whatever suggestions and instructions they put forth. In this way, they

[60] From Arabic; meaning 'lord'.

may be *deferentially* vulnerable to the researchers and their proposal. Put differently, that it is coming from people who are highly educated medical professionals attaches to the (objectively non-coercive) suggestion that the donors give samples a much different value had it come from someone who lacked these attributes – in a way that may in fact constrain the donors' subjective view of their options (i.e., their beliefs about options and their values). This echoes Kamyua et al.'s findings from their studies of consent processes in Kenya:

> *"Contextual factors […] are often the most dominant influences on voluntariness in informed consent […]. Typical examples in our setting are that patients or research participants may find it difficult to say "no" to doctors or researchers, and community members may want to say "yes" to a local researcher because they are friends of the family"* (Kamuya et al. 2011, pp. 31-32).

Viewed through this lens, we can see that the donors in this particular situation acquire several *layers* of vulnerability. None of the features of their situation or psychology make them inherently vulnerable, but combined with the way researchers choose to navigate in these circumstances may *render* them so: all the circumstances may add up in a way so that the donors view their option to decline participation in research as unreasonable (even though this is not objectively so). On Liberto's account, this is the stuff that exploitation is made of. Here, recall my qualification that what qualifies this as exploitation is that the exploiter must a) know that the exploitee will view her options in a certain constrained light, and b) use this to his advantage.

So, equipped with this more nuanced way of regarding vulnerabilities vis-à-vis exploitation, we are finally able to ask whether our Pakistan case is one of exploitation. We can answer this in the positive if the researchers knowingly take advantage of the fact that the donors' specific layers of vulnerability will make them view their refusal as unreasonable (even though it is not). In what follows, I will argue that there is a plausible case for claiming that this is so.

As is customary, the researchers approach the elders of the families for consent on behalf of the family members. When that of the elder is the only consent given, it is impossible to know whether any of the family members had any reservations against participating, i.e. that their compliance was an expression of their willingness to participate or merely compliance to elder authority (or both). Now, it is not unreasonable to claim that researchers could have done something to tease out the 'true will' of the other family members.[61] However, a potential consequence of this could be that these individuals in question say no to participation, resulting in fewer samples for the researchers' work. Hence, if the researchers stick to only having to convince one person (the elder), knowing that if he is convinced, the rest of the family will fall in line regardless of their own potential reticence they researchers exploit the individual donors' obedience to their elder.

Furthermore, since the researchers are from and/or familiar with the area they operate in, we have good reasons to assume that the researchers are aware of the donor population's general deference to certain people, namely medical professionals. While letting the family know that their participation is fully voluntary, they also indicate that they are medical professionals carrying out the research. By disseminating these bits of information, the researchers play into the donors' particular deference to particular people, so that the relation adds up in a way, specific to these donors, where they are *less inclined* to say no: you simply do not, at least as easily as with laymen, say no to medical professionals. In this way the researchers leave the door wide open, so to speak, but also place certain very specific obstacles so that it to the donors seems if not closed, then at least out of reach. We may then claim that the researchers exploit the particular psychological and deferential profile of the donors, to get them to respond and act in a certain way.

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[61] Aamir Jafarey (2003) has suggested ways to incorporate the role of the family in this particular context in the consent process.

I have now made the case that the researchers do in fact exploit the donors if and when they knowingly take advantage of the donors' vulnerabilities, i.e., the ways their decision-making capacities are impaired by the particular characteristics of them and the research situation. To the extent that this is the case, our research case can rightfully be called one of exploitation. Nevertheless, it is one that pales in comparison with the cautionary and horrendous examples of exploitation in medical research usually brought forth in the literature:[62] the are no grave side effects, no serious deception, no coercion, and no unfair distribution of benefits. Thus it may be reasonable to ask, then, if it *is* a case of exploitation, is it really that serious or harmful, compared to some of the other known cases? Probably not. But this would miss the point: as we have seen (with Wertheimer, for instance), there can be exploitation that does not *harm* the exploitee in the usual sense; however, this does not take away from the fact that it is still very much exploitation. This seems to be precisely so in our case. However, the very fact that it is a case of exploitation to begin with is overlooked if we do not take a much more nuanced approach to vulnerabilities in relation to exploitation; as I have done in this last section.

6. Conclusion and outlook

This paper was inspired by the uneasy intuition that there was 'something fishy' about the Pakistan case; something that smells like exploitation. The aim of this paper, then, has been to explore and determine whether the case of the Pakistani biobank donors was one of exploitation – that is, whether the researchers exploit the donors, and if so, in what sense(s). To accomplish this, I have analyzed the case from the point of view of the standard theories of exploitation (Kantian, unfairness-centered and circumstance-centered). As an overarching result, on these theories the case is not one of exploitation.

This is not satisfactory, however – it seems that there are features of this particular case that appear as potential grounds for exploitation; nonetheless these are not sufficiently captured by the standard theories. We thus need a much more nuanced and fine-grained view of what can serve as grounds for exploitation, i.e. vulnerabilities.

A refined vulnerability view such as those put forth by Kipnis, Luna and Liberto, respectively, seems to do the trick: as it understands vulnerabilities as a function of the particular interplay between the specific characteristics of the situation and the people in it and how this may impair the potential exploitee's decision-making capacities, this highlights vulnerabilities for exploitation that stay hidden from view if we solely focus on the circumstances (or the characteristics of the people involved). This allows us to see how the how the donors in our case in this particular setting acquire very specific vulnerabilities – e.g. deference to doctors or highly educated people – and in turn how this opens up an particular avenue for exploitation.

As I have suggested, as a modification of Liberto's view, whether exploitation does in fact occur is a question partly separate from this, and the response requires putting under close scrutiny how the potential exploiter responds to these particular vulnerabilities, in our case how the researchers interact with the donors and their situation and psychology. And in our case we seem justified in saying that they respond to the donors in a way that can qualify as exploitation under this conception.

[62] Examples include the cases of Henrietta Lacks (see Skloot 2010), the Tuskegee syphilis study (see e.g. Jones 1993), the case of the Havasupai Tribe (see Van Assche 2013), and the Havrix and Surfaxin Trials (see Hawkins & Emanuel 2006).

As I have noted elsewhere, however, whether non-harmful and beneficial exploitation is morally wrong is a contested issue. And although my analysis does answer the question of whether our case is *exploitative*, it still leaves at least partially open the question of whether the sort of exploitation that takes place here is *morally wrong* (assuming, of course, that we do not conceive of exploitation as being morally wrong per definition). Answering this question would warrant an investigation in length equal to the preceding one, so this is an endeavor I will save for a later time. However I believe my systematic account of and analysis from the different families of theories of exploitation has done some of the groundwork (more specifically, I believe it puts us in a position to stipulate that Wilkinson, Sample and Wertheimer would answer that our case of exploitation is not morally wrong, whereas Goodin, Valdman and Liberto would answer that it is).

As instructive for further investigation (both that of others and my own), I will point to a claim that I deliberately, given the focus of this paper, have not given much consideration: namely, as e.g. observed by Goodin, an act of exploitation is always a wrong (because it implies treating another in a wrongful/unfair way), but not always one that is wrong on balance to perform (Goodin 1987, p. 173) – in other words, there may be good moral reasons why we should allow acts and practices that we in fact consider exploitative. David Resnik has raised this point vis-à-vis biomedical research specifically, stating that *"describing a study as exploitative does not definitively settle questions about the morality of the study"* (Resnik 2003, p. 234), and goes on to urge that the morality about a given research project must be determined by asking further questions about a) its potential for and balancing of harm, disrespect and injustice, and, should these be determined to be minimal enough, b) whether the research project is morally justifiable in spite of its exploitative features. He concludes that *"it is likely that a great deal of bioethical research is minimally exploitative yet still morally justified"* (ibid., p. 252). This dilemma is echoed in the literature discussing whether and to what extent we may legitimately interfere with such research arrangements. In particular it has been stated that in the context of research with developing countries and/or with populations that may have been categorized as vulnerable we may in fact have strong overriding moral reasons *not* to interfere with research that has exploitative features. For instance, some mutually advantageous exploitative arrangements may present the research subjects with access to help and support that they would not have had access to otherwise.[63] Entering into this exploitative arrangement thus represents the best course of action for the research subject, compared to a no-transaction situation. Prohibiting participation may thus rightly be viewed as being highly paternalistic, and, as some commentators have noted, placing a disproportionate weight on the principle of non-maleficence at the expense of other important principles in medical ethics, such as beneficence and individual autonomy (Schrems 2014). It may even make the situation worse for the research subject: as Christine Grady has argued, *"'protecting' people by denying or limiting their access to desirable goods may serve simply to limit their options, and may increase their vulnerability to possible exploitation"* (Grady 2009, p. 24). This is an effect Lange et al. (2013) have termed *pathogenic vulnerability:* the creation or exacerbation of new vulnerabilities created by efforts to alleviate existing perceived vulnerabilities (an example is the exclusion of pregnant women from research as an act of protection resulting in a lack of empirical evidence of the effects of certain drugs in pregnant women, which may harm other pregnant women).[64]

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[63] The 2000 Surfaxin trial in Bolivia can be said to be of this type. A private U.S. drug company tested their drug for alleviating RDS, Surfaxin, on 650 premature infants at risk of dying from respiratory distress syndrome. The infants were given endotracheal ventilator support with either Surfaxin or a placebo drug. The ventilator treatment in itself, including either of the treatments, was known to improve general survival and was thus better than the treatments generally available to both groups prior to the study. See Hawkins & Emanuel (2008), pp. 58-61.

[64] I am grateful to Katla Heðinsdóttir for further enlightening me on this debate.

While I do recognize the merits of this line of reasoning, I also believe this (largely consequentialist) approach holds the danger of reducing talk of exploitation in research to a Wertheimerian calculation of harms and benefits, and thus leading us full circle back to overlooking subtle, local features of each research case that in fact have significant effects on how research subjects' are and feel pushed into research participation. Appropriate responses to research cases that may be exploitative, then, seem to require careful attention to *both* how the features of each case may in fact justify exploitative arrangements, *and* how certain features of the same case may compromise the efficacy of consent to such arrangements. This is an avenue of investigation I find highly timely to pursue further.

7. Policy implications

The preceding has been a study and analysis of one particular case, however my discussion and findings highlight an issue regarding exploitation that is increasingly recognized as highly problematic in this type of medical research in similar settings. What makes someone vulnerable to exploitation in a research situation is highly dependent on specific local features of the case and, as my discussion has also showed, how such vulnerabilities are expressed can vary widely from one cultural setting to another. If researchers are not acutely aware of such particular local features of the context in which the research is being carried out, many sources of vulnerability risk flying under the radar (as, I have argued, it is the case with both standard theories of exploitation and existing guidelines for research).

This has implications for current policy. I agree with Kipnis and Luna that a more appropriate and adequate way of addressing potential vulnerabilities in research requires a two-pronged effort[65]:

1) *Thorough identification and analysis of all present vulnerabilities in the given research context.*
   This requires not only regarding the potential risks and benefits of the research and the attributes of the population, but also a competent analysis of the broader social and cultural context and scrutinizing the specific research protocol in this light. This includes being acutely aware of any elements of the research protocol and research environment that may affect the particular subjects in a certain way, e.g. certain types of verbal and symbolic communication that may prompt a certain response from certain subjects (as has been made clear from the above, being invited to participate in research by respected doctor or another highly regarded individual may have an impact on the subject's decision-making capacities, or may affect the option-set that the subject is faced with).
2) *Developing appropriate measures to accommodate each type of vulnerability*.
   This step requires developing an appropriate response to each vulnerability identified through the analysis above. Here, it is important to note that each may require a different mechanism for its neutralization with respect to exploitation, and may address different levels of the research. As examples, Kipnis notes that mechanisms that may accommodate juridic vulnerability may include devising a consent procedure that will adequately insulate the individual from the hierarchical system and its juridic powers, and mechanisms that accommodate deferential vulnerability may include paying attention to the conversational setting and devising a procedure that eliminates as much as possible of the social pressure an individual may feel she is under (even if this is not the case).

This is no doubt an extensive undertaking, and requires a significantly increased and more intensified effort on the part of policy makers, IRBs and the like; compared to current standard procedures. Nonetheless, seeing that the preceding lengthy discussion has demonstrated that both standard

[65] See also Hurst 2008 pp. 198-199 for an example of application of this approach by an IRB.

philosophical theories of exploitation and current guidelines for avoiding it fail in adequately addressing, capturing and accommodating the myriad and highly contextually dependent ways research subjects may be vulnerable, this is a hill we are forced to climb if we are serious about wanting to understand and avoid exploitation of research subjects.

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Concluding remarks

Theoretical conclusions

As stated in the introduction, this dissertation explores the concepts of trust, consent, exploitation and vulnerability, and their interrelation in the context of medical research. The vehicle for this investigation was the empirical study of motivations, experiences and expectations among biobank donors and researchers in rural Pakistan.

Where Article 1 detailed this empirical study, Articles 2 and 3 explored the above concepts in a largely pairwise manner: Article 2 analyzed the proper role of *trust* in *consent, and* Article 3 discussed the nature of *vulnerability*, and offer a novel way to view this in relation to *exploitation*.

Taken together, Articles 2 and 3 argue for the following: in contrary to what many standard theories in medical ethics claim, consent to participation in medical research based on trust is not less prudent or robust than consent based on information – thus, such trust-based consent is, in itself, morally defensible. But consent is not all: even where consent to participation in medical research is valid, there may be other factors that make a certain case ethically problematic – for example, makes it exploitative. What makes a case exploitative is that individuals' vulnerabilities are taken advantage of, and what makes individuals vulnerable is that certain circumstances in their situation have a negative effect on their decision-making capacities, and in turn their consent.

As a general conclusion of this dissertation, then, I offer that a conception of consent to participation in medical research that is based on trust is morally defensible; however, this in turn increases our obligations with regards to attention to other factors that may impair or otherwise negatively influence participants' capacity for consent.

Practical perspectives

This project combines philosophical and empirical/sociological methods. This is fairly unprecedented within the discipline of academic philosophy; however, I believe that there are several valuable merits to this approach, especially in the areas of medical ethics and bioethics.

Letting the philosophical work be informed by empirical data ensures that the ethical issues with which one engages are in fact the ones that are most relevant in the particular case. As was the case in this project, the ethical and philosophical issues that are in fact the most pressing and relevant to a particular case may be very different from those one has found to be relevant from a purely theoretical perspective. This of course has a bearing on the quality of one's theoretical work (if we, in spirit of reflective equilibrium, hold that the closer a theory's fit with reality, the higher its quality), but it also has an important practical dimension. As a great deal of work in medical ethics and bioethics (on some level) aims to inform concrete practices and policies, it is of great importance that the issues one's theoretical work addresses are in fact the ones that are relevant in each particular case. If the theoretical work addresses issues that are not relevant in the actual case, then policies and practices based on this work will also miss the target. In contrast, I argue, rooting philosophical analysis and discussion in empirical data ultimately may make for decisions and policies that are a better fit with reality than ones that are uninformed by it.[66]

[66] This relates to lessons offered by Grounded Theory, see Section 4.1. in the introductory chapter.

Empirical data may also inform philosophical theory on a more abstract level. An important element in moral theory is that of *intuitions* – we see this, e.g., in the discussion of reflective equilibrium (see above). However, it seems plausible that intuitions about hypothetical cases can be vastly different from intuitions about actual experienced cases. For example, one may hold the general moral belief that it is wrong to give money to homeless people; however, when finding a barefoot and hungry homeless child at one's doorstep be gripped by the urge to give her money for food (and think of this as the right thing to do in the situation). In this way actual experiences may influence one's moral intuitions, and one may gain certain intuitions only by being in a certain concrete situations. In this project, this was the case with the issue of *exploitation*. In our initial discussions (prior to the empirical study) of the research setup at NIBGE and what might be ethical issues in this context, we did not think of the setup as an exploitative one. However, witnessing the relations and exchanges between donors and researchers pushed our intuitions in a different direction. In this way, "getting one's hands dirty'" with empirical work may alter (and potentially improve) one's moral theory.

Conversely, philosophical methods may have a lot to offer empirical and sociological work – both within and outside the scope of bioethics and medical ethics. In this project, the empirical study was preceded by a mapping of the ethical issues pertaining to the field of biobanking and research in developing countries, followed by a discussion rooted in moral philosophy of the nature, importance and relevance of these issues. This played an important and valuable role in informing and shaping the interview guide: what are the most important issues to pursue, from a philosophical point of view? How can we word questions to donors that will properly elucidate these often very abstract concepts, such as autonomy and trust? Particularly the latter question showed the value of conceptual analysis and clarity in developing interview guides. One all-important lesson here was that defining the conceptual contours of any concept one wishes to investigate is a prerequisite for developing questions that may elucidate it in a satisfactory manner. Only by being extremely clear on what exactly we understand by (e.g.) autonomy, and in turn how this concept are expressed in individual action and decision-making, we were able to develop and ask questions that explored exactly this.

Summary

This dissertation investigates ethical issues that arise in biobanking (i.e., the systematic collection and storage of samples of human material for research) across national and cultural borders. Building on an empirical study of the expectations, motivations and strategies of biobank donors and researchers in rural Pakistan, the dissertation examines four concepts that are relevant in this context: trust, consent, vulnerability and exploitation.

The dissertation consists of three articles, preceded by an introductory chapter showing how the articles relate to my main topic and the ongoing ethical debates in this field.

In the introduction I first set the scene for my investigation by giving an account of relevant features of the societal and ethical landscape in Pakistan, and of the nature of biobanks. I then discuss the various ethical issues that have been raised regarding biobank research and medical research in developing countries, respectively; focusing on the issues of informed consent and exploitation.

Article 1 details the empirical interview study conducted with biobank donors and researchers in rural Pakistan. The study found that central to the decision to consent to give blood samples for research was the trust they held in the researchers – either as interpersonal, institutional or indirect trust. In addition, the study found that in order to gain the trust and cooperation of donor families, researchers in the field often modify standard ethical requirements for informed consent to the local circumstances, and employ alternative strategies for obtaining consent.

Article 2 examines the moral value of this sort of trust-based consent. The practice of informed consent is a cornerstone in medical ethics, as the provision of information about a given intervention or study is held and hailed to be the optimal way to protect and promote the autonomy of patients and research participants, and protect them against coercion, manipulation and exploitation. This attaches a significant moral value to information and decisions made on the basis of it. In the article we analyze whether these values underlying the ideal of informed consent (autonomy, voluntariness, non-manipulation and non-exploitation) are protected to a lesser extent by trust, as compared to information. We find that this is not the case, and argue – in contrast to the common claim in medical ethics – that trust-based consent is not morally inferior to informed consent. We conclude by discussing the implications of our argument for current medical ethics.

In Article 3 I investigate whether the case of sample collection for biobanking detailed in Article 1 is one of exploitation; that is, whether the donors are being exploited in any sense, and if so, what features of the case make it so. I do this initially by analyzing the case from the point of view of standard theories of exploitation (which I group into Kantian; unfairness-centered, and circumstance-centered theories). Generally, this analysis shows that the case is not one of exploitation. However, I argue that this result is unsatisfactory, and that the consulted theories are inadequate in that they overlook relevant features of the case that might be grounds for exploitation. I suspect that this is because their conception of vulnerability is overly fixed and narrow. Hence, I then analyze the role and nature of vulnerability in relation to exploitation and consent, and on this basis suggest a more refined and contextually sensitive conception of vulnerability in exploitation.

I wrap up the dissertation by offering some general conclusive remarks and perspectives based on my findings, and by briefly reflecting on how philosophical and empirical research methods may complement each other.

Resumé

Denne afhandling undersøger etiske udfordringer der opstår når biobanker (dvs., organiserede indsamlinger af humant materiale til brug i forskning) opererer på tværs af nationale og kulturelle grænser. På baggrund af et empirisk studie af motivationer, forventninger og strategier blandt biobankdonorer og –forskere i det landlige Pakistan, analyserer og diskuterer afhandlingen fire begrebslige områder der er relevante inden for denne kontekst: tillid, samtykke, sårbarhed og udnyttelse.

Afhandlingen består af tre artikler, samt et introduktionskapitel der viser hvorledes de tre artikler relaterer sig til det overordnede emne og de igangværende etiske diskussioner inden for dette felt.

For at situere min undersøgelse beskriver jeg i introduktionen først relevante aspekter af det samfundsmæssige og etiske landskab i Pakistan, samt vedrørende biobanker som praksis. Med henblik på at relatere mit projekt til de forskningsfelter det grænser op til, diskuterer jeg hernæst visse etiske problematikker der er blevet rejst i diskussioner om henholdsvis biobankforskning samt medicinsk forskning i udviklingslande.

Artikel 1 redegør for den empiriske interviewundersøgelse med biobankdonorer og –forskere i det landlige Pakistan. Undersøgelsen viste, at et centralt element i donorerne beslutning om at give samtykke til donation af blodprøver til forskning var den tillid de havde til forskerne – enten i form af interpersonel, institutionel eller indirekte tillid. Undersøgelsen viste ydermere at forskerne ofte modificerer standardkravene og –procedurerne for etisk samtykke til forskning ud fra de lokale omstændigheder, med henblik på at vinde donorfamiliernes tillid, og herigennem deres samtykke til at give blodprøver.

Artikel 2 undersøger den moralske værdi af denne type tillidsbaseret samtykke. Informeret samtykke er en hjørnesten i medicinsk etik, idet det antages, at det at give patienter og forskningsdeltagere information om en given intervention eller undersøgelse er den optimale fremgangsmåde til at beskytte og fremme deres selvbestemmelse, samt beskytte dem mod tvang, manipulation og udnyttelse. Således bliver information, og beslutninger taget på baggrund heraf, tildelt en høj moralsk værdi. I artiklen analyserer vi hvorvidt tillid beskytter de underliggende værdier i informeret samtykke (autonomi, frivillighed, fravær af manipulation samt af udnyttelse) til en mindre grad end information. Vores analyse viser at dette ikke er tilfældet, og vi konkluderer derfor – i kontrast til den dominerende påstand i medicinsk etik – at tillidsbaseret samtykke ikke er af moralsk ringere værdi end informeret samtykke.

I Artikel 3 undersøger jeg hvorvidt indsamlingen af prøver fra de pakistanske donorer (redegjort for i Artikel 1) kan beskrives som udnyttelse, og i så fald hvilke faktorer der bidrager hertil. Dette gøres ved indledningsvist at analysere casen ud fra standardteorier om udnyttelse (som jeg grupperer i henholdsvis Kantianske, uretfærdigheds-, og omstændigheds-orienterede teorier). Overordnet set viser denne analyse at casen ikke kan beskrives som udnyttelse. Jeg argumenterer imidlertid for at dette resultat er utilfredsstillende, og at de anvendte teorier er utilstrækkelige i og med at de overser visse aspekter af casen, der kan være basis for udnyttelse. Jeg mistænker at dette skyldes at begrebet om sårbarhed i disse teorier er for snævert og rigidt. Derfor foretager jeg hernæst en grundig analyse af begrebet om sårbarheds natur, og dets relation til udnyttelse og samtykke. På denne baggrund fremsætter jeg et forslag til mere raffineret og kontekstuelt sensitivt begreb om sårbarhed i udnyttelse.

Jeg afrunder afhandlingen ved at fremsætte nogle generelle konkluderende bemærkninger på baggrund af mine fund, samt nogle refleksioner over hvorledes filosofiske og empiriske forskningsmetoder på frugtbar vis kan supplere hinanden.

Appendix 1: Interview guide, Pakistani donors

1. *Can you tell me about the condition that is in your family?*
   - *Why is this condition in your family?*
   - *What do you know about the condition?*

2. *Can you tell me about how you came in contact with this institute?*
   - *How were you contacted?*
   - *What did you talk about?*
   - *Did you know anything about this institution before?*

3. *Now I would like to hear about the process of giving your blood sample.*
   - *What happened when you met with the [doctors]?*
   - *What made you feel that it was ok to give a blood sample?*
   - *How do you know that the people who came to you were to be trusted?*

4. *Can you tell me about how it was decided that you should give a blood sample?*
   - *Who made the decision?*
   - *Did the doctors seek permission from someone else (in your family)? Could they have overruled your decision?*
   - *Was there a written form? What language? Did you read it? Were you able to read it or did you rely on what was narrated to you?*
   - *Did you ask any questions before agreeing?*
   - *Did you have any doubts or apprehensions about giving your blood sample?*

5. *Did you talk to [contact person] about what your blood test would be used for?*
   - *Do you remember anything about your reactions?*
   - *Is there anything you would have liked to know?*

6. *What if your sample could be used to cure someone else's condition – how would you feel about that?*
   - *What if you didn't get a cure, but your sample could help in someone else's cure?*

Appendix 2: Interview guide, NIBGE researchers

1) *What are NIBGE's a) requirements and b) practices for consent, when sampling donors for research?*

2) *How would you characterize the way consenting to giving a sample matters to donors?*

3) *What, in your experience, is most important for the donors?*

4) *How do donors balance their interests in treatment and research, respectively?*

5) *How do you experience the level of trust the informants have in a) you as a researcher and b) the institute?*
    - *How is this expressed?*